THE PRACTITIONER

No. 1085 NOVEMBER 1958 Volume 181

THE MONTH

The Symposium

QUO TENDIMUS? Such is the question that an increasing number of the public is asking as the scientists unleash the hitherto untapped sources of energy in the atom. Human nature being what it is, the emphasis is upon the hazards to life and health involved in this scientific revolution. General practitioners are now encountering a growing proportion of patients who are seeking information on this matter. Unfortunately, the information available is scattered throughout the specialized journals, is highly technical in character and, all too often, contradictory. This last feature is particularly noticeable in the case of the writings of certain atomic scientists who have forsaken the seclusion of their laboratories for the public platform or the public press.

It is in order to supply our readers with an authoritative and straightforward review of the present state of knowledge on the subject that we have devoted the symposium this month to 'Radiation Hazards'. We are grateful to the contributors—all leading experts in their subjects—for having spared the time to assist in the preparation of this guide to the subject. They would be the first to admit that they have not provided all the answers to all the questions—simply because these are not yet available. What they have done is to summarize the present state of knowledge and to indicate the hazards that are involved. The composite picture they present is, on the whole, a reassuring one. Atomic energy is as potent for evil as for good. The hazards, however, are well—if not fully—appreciated, and the public can rest assured that everything humanly possible is being done in order that they should be reduced to an irreducible minimum.

Russian Medicine

IT is still far from easy to obtain anything like a clear idea of current methods and standards of medical practice in Soviet Russia. One day, perhaps, the iron curtain that is so foreign to traditional views of medical cooperation will be raised. Meanwhile all that we on this side of the curtain can do is to study the occasional items of news that are allowed to percolate through and hope thereby to obtain some idea of how medicine is practised on the other side. From this point of view a report of the fifth Congress of the Medical Workers' Trade Union that was held in Moscow this summer is not without interest.

According to this report, the Soviet Union has more doctors per head of the population than any other country, but they are very unevenly distributed, ranging from 30 doctors per 10,000 population to 30 doctors per 6000 population. The staffing of village medical centres is particularly unsatisfactory, and the Ministry of Health and the central committee of the Medical Workers' Trade Union are being accused of not having been energetic enough in rectifying errors in the training and posting of young doctors. That all is not well is indicated by the fact that the presidium of the All-Soviet Trade Union Council has drawn attention to the delay in fulfilling the plan for the building of medical centres. So unsatisfactory is the position in this respect that recourse has had to be made to old-fashioned private enterprise, and with their own resources and at their own expense collective farmers are building crèches, maternity homes, and houses for medical workers. The comment that medical and trade union authorities are still insufficiently concerned about improving working conditions for doctors will strike a sympathetic note at B.M.A. House, whilst the Medical Research Council will be able to sympathize with their opposite numbers in Russia on learning that the trade union branches of the Academy of the Medical Sciences of the U.S.S.R. and its research institutes were 'sharply criticized' for not doing more about the prevention of diseases such as tonsillitis and influenza.

Harvest Thanksgiving

THE dead hand of bureaucracy is one of the spectres haunting the National Health Service. Indeed, in some respects it is the fundamental criticism of the whole concept of a National Health Service. Fortunately, our national genius for resisting regimentation still survives and, in spite of all the machinations of the bureaucrats, voluntary service continues to play an important part in humanizing the Service. In fairness to those responsible for the Service it should be noted that successive Ministers of Health have paid tribute to the many contributions that voluntary service has made. Unfortunately, these excellent precepts have not always been carried into practice by their underlings.

A disturbing example of what can only be described as bureaucratic ineptitude is referred to in the October issue of *London Churchman*, the official publication of the Diocese of London. This concerns the disposal of the fruit and vegetables presented to churches for their Harvest Thanksgiving Services. In the old days no problem existed. After the services these were taken to the local hospital, or hospitals, where they were thankfully received. 'But today', to quote the editorial comment in the *London Churchman*, 'the entire National Health Service cannot, presumably, so organize its budget as to allow for an autumnal vegetable flood and for a period of a fortnight during which nothing but vegetation of one sort or another appears on the menu. Hospitals, then, are "off" '. This is a state

of affairs for which there is no excuse. Unless the principle is firmly maintained that hospitals exist for the benefit of patients, not the convenience of administrators, the outlook for the sick citizen is indeed bleak. That these thank-offerings from the churches of the country should be refused by hospital authorities is the antithesis of the spirit of charity and service which has always been the glory of the practice of medicine.

Adolescent Blood Pressure

As Professor J. C. McClure Browne pointed out in our June issue (p. 651), 'although maternal death from toxæmia is almost entirely preventable by proper antenatal care there is clear evidence that toxæmia is still the major cause of death among childbearing women in this country, and in 200 deaths from this condition during 1952-54 avoidable factors were clearly present in over 50 per cent.'. Among women particularly prone to toxæmia are those with a hypertensive tendency, however mild, and the early detection of this group would go far towards reducing this unnecessary maternal mortality.

For this reason particular attention is due to a study of blood pressure changes in adolescent girls by Leo Hahn (*Med. Offr*, 1958, **100**, 97), based upon a follow-up study of 60 girls attending a secondary modern school in Leicester, in which the systolic blood pressures were compared at the ages of 12.25 and 14.25 years. This showed that the average rise of systolic blood pressure was 5.8 ± 2.4 mm. Hg, and that this was more clearly connected with increase in height than with increase in weight. The important implications of this study, however, are that once maturity has been attained a girl reaches her adult blood pressure, and that 'each girl has her own law for her individual norms'. Hahn quotes two examples of what this means later in life. A woman who, mature at the age of 14, had a systolic blood pressure of 90 to 95 mm. Hg must be considered hypertensive if at her first antenatal visit she is found to have a pressure of 115 to 120 mm. Hg. On the other hand, a woman whose pressure at the age of 14 was 130 to 140 mm. Hg, and this was well in keeping with her physique and development, need not necessarily be regarded as pre-eclamptic if her first antenatal examination reveals a pressure of 140 mm. Hg. The difficulty, of course, is that so often the adolescent blood pressure is not known, but this is an aspect of preventive medicine which clearly deserves more careful attention than it has received in the past.

Joan of Arc

Doctors and laymen, believers and disbelievers, have wrangled interminably over the explanation of the visions and voices of Joan of Arc. Professor John Butterfield and his wife (*History Today*, 1958, **8**, 628) have now come forward with a most impressive array of evidence suggesting that a tuberculoma in the region of the left temporosphenoidal lobe was the responsible lesion. The evidence in favour of her having a lesion in this region of the brain is that at the age of twelve

she began to have mixed sensations of sight and sound, coming from her right, together with sensations of touch and smell. At first these sensations occurred two or three times a week but by the time of her trial, when she was eighteen, they were occurring two or three times a day. The evidence in favour of the lesion being a tuberculoma is rather more indirect. Bovine tuberculosis was rampant in those days and as a child Joan must have had every chance of becoming infected. Further, she had amenorrhoea, which is a recognized complication of tuberculosis in adolescence, and the evidence of one of the doctors who examined her while she was in prison suggests that she had a renal infection which might well have been tuberculous. Finally, her executioners reported that her entrails would not burn and, as the Butterfields point out, this 'would not be surprising if there were many calcified lymph glands in the abdomen, the usual result of bovine tuberculosis'.

The sceptics amongst us, however, must not assume that such a diagnosis explains the 'Maid's' greatness. The Butterfields are careful to point out that 'though we may understand the reason for her visions, we should be making a great mistake if we attributed Joan's greatness to organic disease alone . . . It is not her visions and voices, but her courage, her intelligence, her ability to get big things done and her struggle for the independence of her mind which distinguish Joan and place her among the great women'.

Guildford Cathedral

TOWERING over the Guildford by-pass as it sweeps towards the crest of the Hog's Back, Guildford Cathedral is now nearing completion. Impressive in its majestic simplicity it has already come to symbolize for many far beyond the confines of Surrey the principles of the Faith which is the basis of our civilization. To doctors it has a particular appeal, not only because Surrey is one of the beauty spots of England, but also because so many of them came to know the county during the last war. During those fateful years the road to Portsmouth became a military highway along which passed convoy after convoy to or from the South Coast, whilst Aldershot and Crookham, just across the boundary in Hampshire, provided many a doctor with his first experience of Service life.

It is therefore a fitting gesture that the Guildford division of the British Medical Association should have decided to issue an appeal to the profession for contributions to a fund to provide one of the lancet windows in the new Cathedral. There must be many doctors, both at home and overseas, who will wish to avail themselves of this opportunity. Donations should be sent to The Doctors' Cathedral Window Fund, c/o The Treasurer, Dr. F. A. Belam, 1 Westfield, Epsom Road, Guildford, Surrey.

THE EFFECTS OF RADIATION ON THE INDIVIDUAL

By J. F. LOUTIT, C.B.E., D.M., F.R.C.P.

Director, Medical Research Council Radiobiological Research Unit, Atomic Energy Research Establishment, Harwell, Berkshire

IONIZING radiations such as X and γ rays release some of their physical energy in their passage through cells and thereby exert biological effects which, so far as we know, are always fundamentally harmful. This is not to say, in the present incomplete state of our knowledge, that they should not be used. The damage that they do may be less than the harm which may accrue from not using them.

As therapy these rays are used in attempts, often successful, to procure complete elimination of malignant cells: and their use here is completely justified. They are also applied to tissues with simple hyperplasia, but in such cases much more thought has to be given in weighing the relative risks. Administration of radioactive iodine may be the treatment of election for the elderly thyrotoxic woman, since the late effects of the treatment may well be postponed until well beyond the expected life span of the patient. For the young thyrotoxic subject, with a sounder myocardium and better able to withstand the immediate effects of operation, surgery may be the preferred treatment because with a long expectation of life there is ample time for the late effects of the radiation to be expressed. In diagnosis, the use of x-rays has undoubtedly been revolutionary. Have the benefits from improved diagnosis, and therefore treatment, been overbalanced by damage due to the X rays? There is no way of suspending the scale in order to measure the relative weights, but informed opinion is overwhelmingly on the side of the benefits conferred. A few special radiological examinations may provide exceptions to the general rule. These are associated with relatively large doses of radiation to a particularly radiosensitive part. Perhaps the best examples were identified by the Medical Research Council (1956) in their report, 'Hazards to Man from Nuclear and Allied Radiations'; they involved chiefly irradiation of the pelvis and the gonads with consequent genetic hazard with which we are not here concerned. Tissues other than the gonads, however, are also in the direct beam and the effects on the individual have to be assessed.

SOME FUNDAMENTAL DATA

From fundamental radiobiology we are confident of certain phenomena:—

(1) The larger the dose the greater the damage. The relationship is simple when gene mutation is being considered; in fact there is a direct proportionality between dose and effect, as shown in fig. 1. Gene mutation is the only effect for which this type of simple relationship is accepted, although

it is not improbable that other effects may obey a similar law. The phenomenon implies that all doses, no matter how delivered according to time, will have an additive effect and that there is no recovery with time.

(2) For other biological effects the rate of delivery of dose is important. Recovery from the effect does occur, so that doses separated in time do not have an arithmetically additive effect and, if during any one exposure the rate of delivery of dose is slow enough, recovery may occur at a rate nearly equal to the damage. Graphically the dose-effect relationship is sigmoid as in fig. 2 and, depending upon dose-rate, the relationship alters. X-ray machines emit their radiations at a very high dose-rate, so that above a certain threshold of dose, below which no effect may be observable even though it is occurring, the degree of effect rises remarkably rapidly. At the other end of the scale, natural background radiation from cosmic sources and terrestrial radioactivity is received at a very low dose-rate and no somatic effects attributable to it have been detected (although we can predict that it does have a gene-mutation effect).

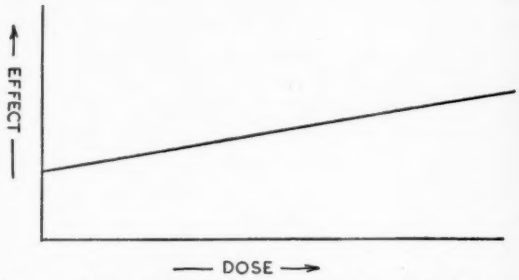


FIG. 1.—Linear relationship between effect and dose—no threshold.

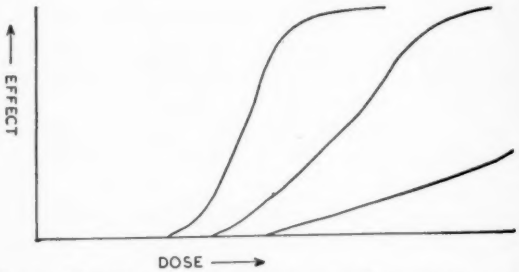


FIG. 2.—Non-linear relationship between effect and dose—no threshold.

(3) The greater the mass of tissue irradiated the greater the effect. Thus, general irradiation of the whole body is much more damaging than irradiation of a mere part. In practice, uniform irradiation throughout the whole volume of the human body is practically impossible to achieve because of progressive absorption of energy with depth in tissue and variation in absorption according to density (bone *v.* soft tissue). It might be thought that a good measure of effect could be obtained from the radiological dose measured in ergs/g. (1 rad is 100 ergs/g.) multiplied by the mass irradiated,

but the calculation of this integral dose is a complex mathematical exercise and does not take into account the following.

(4) Tissues vary in their radiosensitivity. As a rule the acute effects of radiation are most readily seen in tissues which are constantly replicating their cells: embryonic tissues, testis, intestinal mucosa, skin and hæmopoietic tissue. Disturbances of the process of mitosis are readily demonstrable with moderately large, acute doses (e.g. 100 rads), but direct cell-death also occurs with these doses and can be seen particularly well in small lymphocytes, which do not normally divide, and ova. The sensitivity of the various tissues for delayed damage is, however, less well documented and much less well understood. The changes that occur are atrophy, fibrosis and neoplastic transformation. Atrophy and fibrosis may well be sequelæ, immediate or delayed, of large doses delivered at high dose-rate and they are, of course, often seen following doses of radiation in the therapeutic range—hundreds or thousands of rads delivered to the treated part.

What we are mainly concerned about here are the sequelæ either of small doses (a few rads or a fraction thereof) of high intensity radiation such as diagnostic x-rays delivered to a part at infrequent intervals, or a chronic exposure of the whole body to radiations, mainly γ-rays, given at low-dose rate. The latter is the situation for adults in occupations involving work with radioactive materials, and for children in the world at large now being contaminated above the natural background with man made radioactive materials. For the occupationally exposed adult the permissible rate of accumulation of dose is now set as an average of 5 rads a year and for any one of the population at large 0.5 rad a year. The question being asked is whether these exposures, diagnostic and environmental, in addition to natural background, will lead to an increased incidence of malignant disease.

HUMAN EVIDENCE

Evidence from human sources is extremely limited and can be classified according to whether the exposure to radiation was local or general.

Local.—Following therapeutic irradiation or accidental radiation-burns, local malignancy has been recorded on many occasions. There is a long latent interval, anything from fifteen to fifty years. The reports have mostly been of skin carcinoma but sarcomas, including osteosarcomas, are known. The inducing doses are poorly documented since the observations are culled from early days, but 1000 rads in divided doses seems certain to be the minimum. Tumours, especially osteosarcomas, are also known to result from deposition of radioactive material in bones.

General.—Leukæmia of most sorts, except chronic lymphatic, seems to have been induced in three categories:—(a) American, but apparently not British, radiologists who must have received in their work widespread irradiation at high-intensity intermittently. (b) Cases of ankylosing spondylitis treated by radiotherapy to the spine and large joints, so that most of the active bone marrow which is in the bones of the trunk must have received

substantial doses intermittently at a high dose-rate and (c) survivors from the atomic bombs at Hiroshima and Nagasaki who received in one flash a large dose of radiation involving the whole body.

Only in the case of ankylosing spondylitis is the dose of radiation adequately documented, but here it is arguable whether to calculate from estimated mean dose or maximum dose to the marrow or the integral dose to the body. Court Brown and Doll (1957) prefer the mean dose to the bone marrow from which they derive a dose-effect relationship which is nearly linear, indicating either no threshold of dose below which no leukæmia was induced or a threshold which at the most is a hundred or so rads. Lewis (1957), speculating on all three groups (a), (b) and (c), postulates that a linear relation between dose and effect is valid and derives an incidence of 10^{-6} cases of induced leukæmia per annum per rad. This postulate implies that induction of leukæmia by radiation obeys the same laws as, and is of similar nature to, induction of gene mutation in germ cells; that is, that it is due to gene mutation in somatic cells. This is a theory of carcinogenesis that has been discussed for many years and found wanting, certainly as a sole cause. There is ample evidence that in many established cancers the chromosomes, in which the genes are carried, are abnormal. This must indicate loss of some genes and perhaps duplication and mutation of others, but the evidence all suggests that this is a secondary and not primary effect. The theory would also require that leukæmia be increased in incidence with increasing age and accumulation of radiation-dose from natural radiation. In fact, certain statistics show that only chronic lymphatic leukæmia increases in this way (Witts, 1957), and this is the only type of leukæmia which historically has not been linked with radiation.

EXPERIMENTAL EVIDENCE

Leukæmia occurs naturally in most species of animals. The exact clinical counterparts of the human diseases are not seen, but this is not to be expected any more than identity of faces. There is sufficient similarity for one to accept that the processes are comparable.

The mouse is the favoured experimental animal for research in leukæmia as for most cancer, because large numbers can be investigated and genetically pure strains are available. Certain strains have been selected for a high incidence of leukæmia and in these selected lines up to 90 per cent. or so die from this disease; usually it is a lymphoid type but some strains have myeloid leukæmia. Even in strains not so selected and in hybrids leukæmia can be readily induced by radiation. Controlled experiments show that this is most easily achieved by irradiating the young rather than the mature, and by giving fractionated doses of radiation at high-dose rate rather than the same over-all dose either in a single burst of high intensity or in the same total time at a low dose-rate. This latter phenomenon is quite unlike what one would predict if the primary lesion was the induction of a somatic gene mutation. Another important finding is that irradiation of the whole

body is markedly more productive than irradiation of a part. Shielding of but a small part of the normal marrow is protective, perhaps because it provides a locus of normal cells from which the rest of the marrow may selectively be repopulated (Loutit, 1957) or maybe because it provides a 'recovery factor' (Kaplan, 1954). Furthermore, in the case of those mice at least which develop the so-called lymphoid leukæmia with an acute course, the thymus which often is apparently the site of origin plays an important part. Early thymectomy prevents the leukæmia in the naturally susceptible strains (Furth, 1946) and in the radiation-induced condition of others (Kaplan, 1950). Kaplan and his co-workers (1956) have made the remarkable observation that a normal thymus re-implanted subcutaneously into the thymectomized, irradiated animal, may enable such an animal once again to develop leukæmia and the site of origin may be the unirradiated normal thymus. This observation has been amply confirmed (Law and Potter, 1956; Loutit, 1958). Kaplan (1958) now postulates that irradiation may act through indirect mechanisms conditioning the animal by a disturbance of its internal environment to select chance mutants, or to undergo abnormal repair, or to activate a latent virus.

The role of viruses in the induction of leukæmia and other neoplastic states is now being widely discussed. It is generally accepted that certain avian neoplastic states are due to virus infection (Rous, 1910). Gross (1958), having found that cell-free extracts of tumorous tissue from mice of a high leukæmia strain, when injected into new-born mice of a normal strain, regularly give rise to lymphoid leukæmia, postulates that leukæmia is due to a virus which is transmitted vertically from a parent to offspring through the germ plasm. Presumably the natural host-strain is thus immunologically tolerant of this agent (Billingham *et al.*, 1956) whilst normal mice develop immunity to it in nature but can be made tolerant if injected when immunologically immature at birth. Myeloid leukæmia can be similarly induced by injection of certain new-born mice with cell-free extracts of a murine sarcoma (Graffi, 1957). Gross's agent can be cultivated *in vitro* in tissue culture: cell-free extracts of this culture when injected into new-born animals of many species result in the early development of multiple primary neoplasms (Stewart, S., *et al.*, 1958). Similar results are obtained by injecting new-born mice with desoxyribosenucleic acid (Latarjet, 1958). A case can be made therefore that foreign nucleic acids, of which viruses and genes are largely composed, if introduced into cells by artifice or accident, can lead to a synthesis of cell constituents which the cell has no genetic power to control: cancer may thus be something like the process initiated by the sorcerer's apprentice, an accelerating and later disordered division in an attempt to keep pace with the synthesis.

DISCUSSION

Leaving speculation aside, experimental evidence suggests that neoplasia is most likely to supervene when repeated hyperplasia is induced, particularly

when there is some disturbance, either local or general, which militates against ordered resolution and repair. Are these the conditions which obtain after local irradiation for diagnostic purposes or from long-continued irradiation of the whole body in specific occupations involving exposure to radiation? The answer would certainly seem to be, in general, 'no', but in particular cases could be 'yes'. Diagnostic irradiations which involve the absorption of doses of the order of tens of rads should only be carried out when absolutely necessary and repetitions still more stringently controlled. Such examinations are particularly those which entail prolonged screening. Others which involve irradiating the fœtus or young children may be more than normally damaging. Stewart, A., *et al.* (1958) have reported that neoplasia in children is somewhat more frequent in those irradiated *in utero* than in the unirradiated. The object of future development should be the reduction of radiological dose delivered for each examination; with an improved technology it should be possible to reduce doses substantially. Meanwhile radiological examinations should be ordered with due caution and selectivity. So far as occupational exposures are concerned, whilst there have been progressive reductions in the last two decades of permissible doses, these have been conditioned more by caution than from objective evidence of permanent damage caused. The latter is conspicuously absent since the 'bad old days' of the radiation martyrs and, whilst some aberrations from the normal, for instance in blood counts, have been reported under more recent conditions, there is nothing to indicate that these have any sinister portent; they might well represent reaction and response to radiation rather than irreversible damage. Certainly experimental animals are not adversely affected by doses of radiation within the permissible range—or even by doses ten times larger.

References

Billingham, R. E., Brent, L., and Medawar, P. B. (1956): *Phil. Trans. B.*, **239**, 357.
Brown, W. M. Court, and Doll, R. (1957): *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 295.
Furth, J. (1946): *J. Geront.*, **1**, 46.
Graffi, A. (1957): *Ann. N.Y. Acad. Sci.*, **68**, 540.
Gross, L. (1958): *Brit. med. J.*, **ii**, 1.
Kaplan, H. S. (1950): *J. nat. Cancer Inst.*, **11**, 83.
—— (1954): *Cancer Res.*, **14**, 535.
——(1958):'Seventh International Cancer Congress, Abstracts of Papers', London.
——, Hirsch, B. B., and Brown, M. B. (1956): *Cancer Res.*, **16**, 434.
Latarjet, R. (1958): *C.R. Acad. Sci. (Paris)*, **246**, 853.
Law, L. W., and Potter, M. (1956): *Proc. nat. Acad. Sci. (Wash.)*, **42**, 160.
Lewis, E. B. (1957): *Science*, **125**, 965.
Loutit, J. F. (1957): In 'Advances in Radiobiology', edited by G. C. de Hevesy, A. G. Forssberg and J. D. Abbatt, Edinburgh, p. 388.
——(1958):'Seventh International Cancer Congress, Abstracts of Papers', London.
Medical Research Council (1956): 'The Hazards to Man of Nuclear and Allied Radiations', Cmd. 9780, H.M. Stationery Office, London.
Rous, P. (1910): *J. exp. Med.*, **12**, 696.
Stewart, A. E., Webb, J., and Hewitt, D. (1958): *Brit. med. J.*, **i**, 1495.
Stewart, S., Eddy, B. E., and Borgese, N. (1958): *J. nat. Cancer Inst.*, **20**, 1223.
Witts, L. J. (1957): *Brit. med. J.*, **i**, 1197.

THE GENETIC HAZARDS OF RADIATION

By ALAN C. STEVENSON, M.D., F.R.C.P.
Director, Medical Research Council Human Population Genetics Research Unit, Warneford Hospital, Oxford

Our understanding of the nature and above all of the quantitative aspects of genetic damage from radiation is still very meagre. Nevertheless, it is perhaps significant that four major reports of groups of scientists who have examined and reported on the problem have shown a surprising unanimity in their conclusions as to the limited deductions which can be made from the knowledge at present available. These reports are the Medical Research Council report (1956) on 'The Hazards to Man of Nuclear and Allied Radiations', the report of the United States National Academy of Science and the National Research Council (1956), the report of the World Health Organization Study Group on 'The Effects of Radiation on Human Heredity' (1957) and the recently published report to the United Nations Assembly by their scientific committee on 'The Effects of Atomic Radiation' (1958).

The arguments followed are rather complex and utilize information from many sources in science and medicine so that it may be useful to follow through in outline the reasoning. The steps are essentially these: the facts of mutation and of induced mutations; the effects of mutations on the individuals who receive them; the ways in which induced mutations spread in, and are eliminated from, populations; the price that individuals pay in that process—the very limited quantitative relationships which we can estimate.

'SPONTANEOUS MUTATIONS'

It has long been realized that mutations or changes occur 'spontaneously' in germ cells. Such changes can pass in the spermatozoa or ova to offspring and will be reproduced in every cell in their bodies including their own germ cells and so could be passed on through the generations. Presumably some of these 'spontaneous' mutations are directly caused by naturally occurring ionizing radiations in a manner discussed below. Others may be determined by chemical mutagens or by chance accumulations of energy within the molecules constituting the essential heredity chemical substances. Some of these changes are gross in the sense that they affect chromosomes as a whole and determine breaks, losses and various other consequent anomalies. Others, which are probably much more important in the radiation context, are termed gene or point mutations. They are believed to occur at the site or locus of a single one of the paired genes on the paired chromosomes. As our knowledge of chromosome chemistry increases and moves rapidly to a point where the chemical hypotheses fit and serve to explain observable

phenomena, as well as for other reasons, it becomes increasingly difficult to speak accurately of a mutation as a change affecting the whole of a single classical gene but the basic argument about 'point' mutations is not substantially affected.

Such mutations once effected are only reversible by a 'back mutation', an event at least as rare as the initial mutation. Such a phenomenon is known to occur in experimental animals. For a variety of reasons, however, requiring rather lengthy explanation, the question of back mutation may be ignored in the present context.

RADIATION-INDUCED MUTATION

Only energy transfer radiations will determine mutations and they will do so in proportion to the energy absorbed. All such energy transfer radiations produce their effect by ionization, either directly, as in the case of radiations consisting of charged particles such as beta or electron radiation, alpha or helium nuclei streams, or by ejection of electrons in the path they traverse when the radiations are not charged (electro-magnetic radiation such as gamma and rœntgen or x-rays of various wavelengths, or neutron streams). It is convenient therefore to use not a physical measure of radiation (the electron volt or 'eV' series) but a measure of the energy absorbed. The rœntgen is the unit most familiar to medical men and is a measure of the amount of ionization produced. It can be applied properly, however, only to dosage of gamma- or x-rays, but for the present purposes it is unnecessary to go into the nomenclature developing in radiobiology.

Induced gross chromosomal damage.—It seems likely that we can afford to ignore gross chromosomal damage, as compared with point mutation damage from radiation, in our present consideration—and for several reasons. In the first place, such severe damage probably usually results either in the germ cell so affected failing to develop or to fertilize, or it determines failure of development of the fertilized ovum at a very early stage. Secondly, chromosomal damage is apparently extremely uncommon at low dosage, even if repeated. On a 'target' hypothesis this can be conceived as requiring that there are two 'hits' of a chromosome within a short interval of time by traversing ionizing tracts. In practice, it has been demonstrated in experimental work that gross damage rises in geometrical proportion to the dosage, starting at a very low level. It is reasonable therefore to concentrate on the phenomenon associated with 'gene' or 'point' mutations; indeed, anxiety is essentially confined to the results of increasing these changes.

Induced point mutations.—The essential change induced at a locus is a molecular rearrangement. It is clear that this can be effected by a single tract of radiation traversing or passing very close to the molecules concerned. There is therefore no dose of radiation, however small, which is not capable of producing the mutation. Or, in a terminology familiar in physiology, there is no threshold. This is a concept of extreme importance in radiation

genetics. If we use the simile of a shot gun and a target, and equate dosage to the number of hits per point or unit area of target, we should expect the chance of a given spot (or gene) being hit by an ionizing trait to be in direct proportion to the number of hits per unit area (the dose). We should therefore expect our relationship between dosage and number of mutations induced to be in direct proportion and, if plotted graphically, to give a straight line or linear relationship. In experimental work in bacteria, fungi, fruit flies and mice this relationship appears to hold within the dose ranges whose effects can be detected and studied. This proviso is necessary because at very low dosages in experiments of manageable size it may be impossible to detect small increases, whilst at high dosage the results are complicated by gross chromosomal damage, somatic effects, sterility and death of the experimental animals. There are other uncertainties but linearity of relationship between absorbed energy and mutations induced is generally assumed.

SIMILARITY OF 'SPONTANEOUS' AND INDUCED POINT MUTATIONS

It is usually assumed, both on theoretical grounds and on the basis of experimental findings, that point mutations whether induced by radiation or naturally occurring are identical (Muller, 1956), and this assumption is implicit in nearly all considerations of the effect of radiation on man. The point is not really susceptible to final experimental proof as, even if a mutation occurring in one way were not detected to occur in the other, it could always be argued, in view of the low frequency of the mutational event, that if observations were sufficiently prolonged an identical mutation would occur in both series of observations.

Further, apart from identity of individual mutations, induced or naturally occurring, there is the matter to be considered of the relative frequency with which mutations occur having differing severity in their effects. There is some evidence that in an allelic series (different mutations which can occur at the same locus) radiation tends to produce the more severe effect mutations (Newcombe, 1952). It has to be remembered, however, that these are the more easily recognized under experimental conditions.

ACCUMULATION OF MUTATIONS IN INDIVIDUALS AND SUMMATION OF EFFECTS OF DOSAGE

It is also usually assumed that the total of induced mutations which accumulate in an individual are in proportion to total previous dosage received, whether that dosage is single or fractional and irrespective of the time over which it is given. Most earlier evidence in drosophila was in accordance with this view and it is a convenient assumption for purposes of making estimates of total dosage and of resultant likely damage. It also has other experimental support in that it would appear, in the male at least, that most mutations are induced in the spermatogonial stage partly because this may be the germ cell stage most sensitive to radiation, partly because even minor

damage to cells at a later stage in the germ line may make them incapable of further development or fertilization: mainly because, at any given time, cells in this stage outnumber all others and are the 'ancestors' of substantially all germ cells which contribute to subsequent generations after approximately a six-week period from any point in time. Russell and Kelly (1958), however, have recently produced some evidence that, in the mouse, large single doses induce more point mutations than the same dosage given continuously over several weeks.

In man, ignoring the hazards of nuclear warfare, we are concerned with the effects on a population of a total dosage reaching individuals in very small amounts. At the present time in this country these are mainly from medical diagnostic radiology and dosage over a short period of time would seldom exceed a unit number of rœntgens per individual. Nevertheless, it is well to bear in mind the possibility that even dosage of this magnitude may, so far as the population is concerned, be of relatively more importance than if the total dosage were averaged over the population.

SEX DIFFERENCES

Another factor which must be considered is a possible sex difference in effective radiosensitivity to mutations, determined by the differing processes of maturation of spermatozoa and ova. It now seems likely that the older view on oögenesis (subsequently doubted) is substantially correct, the essential point in this context being that all ova which subsequently mature in a woman were present in her ovaries when she was born. The resting phase in the ovary may be relatively insensitive to radiation and in any event there are fewer opportunities for copy errors at cell division before maturation than between resting spermatogonia and spermatozoa. In addition, there is, of course, a greater shielding by body tissues of the ovaries than of the testes.

Carter (1958) has recently shown for mice that, at least in one large experiment, mutations induced by acute radiation in female mice is of the order of ten times fewer than those induced in male mice for the same dosage to the area of the gonads. Haldane (1956) has suggested that there is evidence in man in at least one condition of a higher spontaneous rate in males but the evidence advanced is strongly disputed by Cheeseman *et al.* (1958).

SPREAD OF MUTATIONS IN A POPULATION

The genetic unit, in so far as the effect of radiation is concerned, is for many purposes a population rather than an individual or even a family. Indeed it is customary to assume that, given a sufficient span of years, there will be so much admixture as to be effectively random so that the population becomes one enormous family. Many mutations persist for many generations in a population because they are mild in their effects or because they are shielded from the effects of natural selection either because they are recessive or because they only determine harmful effects when they are associated with other mutations (see p. 566). Thus, in time such mutations, however

they originated, spread throughout a population. It follows that for many purposes it is reasonable to assume that, however initial radiation dosage is distributed in the individuals in a population, the figure of importance is the average amount of radiation received by the people in each generation.

THE EFFECTS OF MUTATION

It has been variously estimated that there are between 5000 and 50,000 gene loci on human chromosomes. We can put these into a number of classes on an arbitrary basis for convenience of discussion.

(1) *Classes of gene loci where the relative frequency of alleles appears to be determined by balanced polymorphic mechanisms.*—This class includes a relatively small number of presently recognized loci where the different genes, only two of which can occupy the pair of loci (i.e. allelic genes or alleles), are recognized by specific test. The best and perhaps only fully established examples are those which determine blood groups. Others are detectable chemically in blood and urine where a similar situation probably holds. It is likely that in the future many more such situations will be recognized. The different combinations of alleles at a pair of loci each confer slightly different chances of survival, or of their owners contributing to the next generation: i.e. in biological terms, different selection values.

It was pointed out on theoretical grounds many years ago by Ford (1945),when he enunciated the principle of 'balanced polymorphism', that this was the natural corollary to the maintenance of relative frequencies of these mutants in populations of similar ethnic origins in similar environment. It was impossible to conceive of even the lowest gene frequency being maintained by mutation alone.

In recent years the association of blood groups and their combinations with disease and with fertility have pointed to the mechanisms by which these relative frequencies are maintained.

The effect of increase in radiation on genes participating in balanced polymorphic systems is difficult to conceive of as serious, if the result is merely to determine mutations from one allele to another at or about the same rate. The initial disturbance of relative gene frequencies would be slight (particularly if the alleles occur in near equal frequencies) and presumably the self-righting mechanisms which determine the polymorphism would operate slowly towards reattaining pre-existing levels. Nevertheless we must presume that for people of given ethnic origins and in a given environment, the proportional representation of alleles in a population is optimal, and that there would be small increased risks to a greater number of individuals in a population by reason of receiving unfavourable combinations of alleles as a result of increased mutations. So that we cannot say that the effects would be harmless. Further, it is not impossible that rare very harmful effect mutant alleles might be induced by radiation, or even that, to be speculative, such alleles occur but are never recognized as they are incompatible with life.

(2) *Loci where mutations occur which are, in their individual effects, detectable because they determine segregating anomalies of varying severity but invariably*

detrimental to their possessors, and whose frequency is determined directly by a mutation.—There are several hundred loci whose individuality we recognize in man because there occur at those loci mutant genes whose effects are such that their possessors are characterized in some way by developmental anomalies, specific degenerative syndromes or metabolic disorders. These cannot be clearly separated because presumably if our clinical pathology and biochemistry of the developing, growing and mature organisms were sufficiently delicate we could probably classify them all as 'metabolic disorders'. We are very ignorant as to whether in man less severe effect and indeed undetectable effect mutations also occur at loci where such severe mutations have been identified, but there are indications that more than one mutation of varying severity of effect may occur at such loci and also that what, in our present state of knowledge, are identical effects may result from mutations at different loci.

If an anomaly is apparent, even if only one locus is occupied by the mutant allele (i.e. the individual is heterozygous for the mutant at the locus), the mutant is termed *dominant*. So that the effect could appear in the immediate offspring of the person in whom the mutation occurred. If, in contrast, there is no recognizable effect when the individual is 'heterozygous' but only when both loci are occupied by the mutant then the mutation is termed *recessive* (the individual being 'homozygous' for the mutant at the locus). Dominance and recessiveness, however, are only conventional terms and are usually relative, intermediate states being the rule rather than the exception.

The frequency of a high proportion of single mutant determined traits has probably varied little over many generations. The precise level of the trait frequency in the population is determined by a state of equilibrium between mutation (tending to increase the gene frequency) and selection (tending to reduce the gene frequency). In the case of recessives the levels of inbreeding in the population must also remain constant. Selection acts by determining that, relative to the rest of the population, the possessors of the trait fail to produce the same numbers of offspring who grow up to a stage at which they in turn are capable of contributing to the next generation. The mechanisms of selection against the characterized individual may be lesser chance of survival to birth, lesser viability thereafter or lesser effective fertility. Fertility in turn may be impaired for biological reasons or for social reasons which determine that people with unusual characteristics or disorders get married relatively less frequently.

If these conditions hold, then a permanent doubling of the mutation rate would ultimately lead to the establishment of a new equilibrium trait frequency which would be double that of the pre-existing level. The time taken to establish the new equilibrium would be from one generation in the case of severe dominant-determined traits whose possessors never survived or had offspring, to perhaps thousands of generations in the case of completely recessive mutants. It is possible to make estimates of the summated

frequencies of such traits by dominance and recessiveness and to estimate the effect of a doubling dose of radiation and this has been done with the data of Stevenson (1957a) in the United Nations Scientific Committee Report (1958). This category of mutations has also been studied extensively in animals, but it is difficult to apply quantitative findings from such work to man.

We have a considerable number of estimates from dominant and sex-linked mutation rates for loci of this class in man.

There are some for recessive mutants but for technical reasons the estimates are subject to such large errors that they are unreliable. Independent estimates for individual loci in different Caucasian communities are remarkably consistent but the range for different loci is considerable. Further, there is little doubt that loci studied represent those at which mutation occurs rather often. This is because the labour of collecting information necessary for calculating rates is very considerable and it is relatively easier to collect information on traits where mutation is a frequent event. The range of mutation rates at loci closely studied appears to be from about 4 to 40 mutations per million gametes per generation. For lists of loci studied and estimates see Penrose (1957) and Stevenson (1957b).

There is a number of loci in man which can be occupied by very harmful recessive mutants where another factor is of importance and where the effect of mutation would be buffered and so not so severe. In these, the homozygote expression is rather common although selection against the possessor of the character is severe. It appears that the reason for the high frequency of the traits is not a very high mutation rate—so high as to replace the very high proportion of mutants lost by selection—but because the effective fertility of the heterozygote, the genetic 'carrier', is increased. This results in each generation of the carriers contributing more than in proportion to the next generation, and over half of their surviving offspring will also be carriers. The best documented example appears to be the mutant determining the sickle cell trait where the heterozygote carrier in endemic *Plasmodium falciparum* malaria areas appears to have a decreased risk to death from malaria in childhood and early adult life (Allison, 1954). A similar situation appears to hold for at least two common recessive conditions in this country where the selection against the trait bearer is severe but where the frequency is nevertheless high. These are fibrocystic disease of the pancreas and deaf mutism.

It will be noted that such systems cannot really be separated from those in the previous category of mutations—the balanced polymorphic systems—the only difference here is that one mutation is recognized at each locus where the homozygote is demonstrably harmful and at gross relative selective disadvantage.

(3) *Mutants whose individual effects are persistently modified by other genes or whose effects are dependent upon more or less chance association in a pattern with other mutants.*—Most of the loci in the body can produce mutations which satisfy this description and it must be axiomatic that the expression of the effect of any mutant is modified by many others and by environmental factors. Nevertheless, we must presume not only that there are mutants

whose expression can sometimes be recognized but at other times is so suppressed or modified as not to be recognizable, but that there are many mutants whose single expression is never recognized. In such instances the effect of increased mutation in trait frequency in a population must be envisaged as much more complex and only predictable, even theoretically, in a few postulated simple situations.

There is increasing support also for hypotheses which recognize that, although there is a series of developmental pathways which amazingly often result in a remarkably uniform developmental end-result, there are hazards to orderly development along any pathway and serious risks of maldevelopment along some. Development is genetically controlled, but factors in orderly development are not necessarily due to single or even multiple individually detrimental mutations although undoubtedly these phenomena occur. It is fairly clear that genes at different loci can act as understudies and take over each other's roles and no two individuals necessarily have the same number of alternative genes at different loci. Indeed, from time to time embryos may arise who by sheer chance of inheritance have no alleles in any locus which are necessary for a particular orderly step in development. Again a chance combination of alleles may be unfavourable not merely by a mechanism of deficiency. Finally there is some evidence that for a given development process either heterozygosity *per se* is essential at a certain number of relevant loci or it may be that heterozygosity increases the chance of there being suitable understudies.

Such mechanisms which are termed 'homeostatic' by Lerner (1954), and 'equilibrium and canalization' by Waddington (1940), are at present ill understood but Neel (1958) has produced suggestive evidence for the role of such mechanisms in determining rather non-specific and heterogeneous congenital malformations in Japanese populations.

It will be clear that estimates of the effects of increased mutation rates in traits determined by such systems would be extremely difficult even if we understood the precise mechanisms involved for specific traits. There would certainly be 'buffering', however, in the sense that doubling the mutation rate even at all the relevant loci would not, as in the case of simple single mutant traits, be followed by doubling of the trait frequencies. It seems more likely that the effects would be rather slight and involve small fractional increments only by determining some specific mutations which had a commanding role in some of these systems.

(4) *Single mutants determining embryonic or fœtal or early postnatal death.*—Experimental work in drosophila and in mice has made it clear that there are 'lethal' mutations—the great majority being recessive—which determine death at some stage in development, there being usually no obvious abnormality or understanding of the mechanisms of gene action involved. Some of these recessives are 'autosomal', i.e. on the ordinary chromosome pairs, and others are 'sex-linked', being located on the X chromosome.

It seems reasonable to suppose that similar phenomena occur in man and that some very early embryo failures at, or shortly after, implantation, which are probably not even recognized as pregnancies, some abortions, and some stillbirths are so caused. There has been no demonstration of the occurrence of lethal autosomal recessives at any of these stages in man, but our armamentarium of investigation is so crude that a considerable

proportion, possibly up to ten per cent. of all abortions and stillbirths, *might* be so caused without being detectable (Stevenson, 1958). Nevertheless we can hardly fail to presume, in the absence of much better evidence to the contrary, that these lethals do occur and further, that most of them probably would ultimately be doubled in frequency if the mutation rate were doubled. There is suggestive evidence for the occurrence of induced sex-linked lethals from the disturbance of the sex ratio on the offspring of heavily irradiated persons (Turpin *et al.*, 1956; Neel and Schull, 1956).

Regarding the effects of such phenomena in a population it seems likely that, with the possible exceptions of a few communities, there is ample reserve human reproductive capacity and it is inconceivable that amounts of radiation received from the peacetime uses of ionizing radiations would determine wastage which could not easily be made good. So that there is nothing to support alarm stories about dwindling and even extinction of the human race from such causes. On the other hand, such wastage is distressing to individuals and, by and large, the distress is in proportion to the stage of development when the product of conception is lost.

In animals also there are specific recessive mutations which determine absolute infertility of the homozygous individual and possibly some which alone or together determine relative infertility. Again we must assume that such mutants occur in man and there is some not altogether convincing evidence of the occurrence of relative infertility in the offspring of consanguineous marriages which would suggest recessive contributing factors. How frequent such mutants are we cannot estimate but they must be relatively uncommon and influence the fertility of a population to a very small extent so that they are not alarming in terms of radiation of populations.

(5) *Loci contributing to the value of multigenic or continuously distributed traits or characters.*—The characters in man which provide the ordinary distinguishing features of individuals are, on the whole, graded and not sharply segregating differences.

They are probably determined by the summated effects of alleles at many loci and in a considerable proportion of them measurements are normally distributed, so that a high proportion of measurements in a population fall just above or below the arithmetic mean value in the population and the distribution is more or less symmetrical.

The simplest model we can conceive is of a situation where there are very many contributing loci and where each makes some plus or minus contribution to the size of the character. Thus the resultant measure of the character (ignoring environmental influences) would be in proportion to the algebraic sum of the contributions.

In practice environmental influences greatly affect such characters but a number of observations of simple measurements such as height suggest that this is the mode of inheritance of the non-environmental components. We must presume also that many of the characteristics of man are influenced by inheritance mechanisms of this type. As this probably applies to such important characters as intellectual ability, emotional stability, and fine skills involving proprioceptive mechanisms, it is clear that it is necessary

to consider the implications of the effects to be expected from increased mutations.

There has been no clearer exposition than that of Mather in the Medical Research Council Report (1956).

He says in essence that, assuming the relatively simple model with a considerable number of contributing alleles and no one allele or small group exerting very marked effects on the specific measurement, the effect of increased mutation would be to alter the standard deviation of the measurement from the mean value, the mean being unaltered. It is difficult to assess what would be the extent of the increased scatter of measurement in a population but in the case of a character such as intelligence (assuming that some measure of it can be devised) this would mean an increase in the proportion of those who come into the category of defectives and an increase in the very gifted. It seems likely that society could absorb the results of such a change if not too drastic, but there are difficult ethical and moral questions involved. Mather, however, feels unhappy about making this simple prediction or rather of accepting the validity of the simple model, and suggests that there are likely to be a few loci at which only severely harmful (in this sense deficiency of intelligence) mutations would occur so that the more likely effect, at least for a very long time, would be to reduce the mean level in the population. Even a slight shift could have severe consequences too elaborate to discuss here.

SOURCES OF RADIATION

Man receives naturally occurring radiation from three main sources. The radioactive isotopes of radium, uranium, thorium and potassium in the earth provide a constant source of penetrating gamma radiation, and there is variation in the amount received, by a factor of at least twenty, in different

Source of radiation	Approximate dose to gonads as a percentage of natural background
Natural background	100
Diagnostic radiology	at least 22*
Radiotherapy	?
Shoe-fitting	0.1
Luminous watches and clocks	1
Television sets	much less than 1
High altitude flying	insignificant
Occupational exposure:	
Radiology and industry	at least 1.6
Atomic Energy Authority	0.1
Fall-out from test explosions	less than 1**

*Subsequent information suggests that the dose to gonads from diagnostic radiology is considerably higher than 22 per cent. of natural background sources, being probably much nearer 100 per cent. Data given in the U.N. Report suggests that for the United States and for France the figure is even higher.

**This figure may have to be increased by a fraction of 1 per cent. as it is now realized that cæsium^{137} can occur in fall-out from nuclear explosions and can be concentrated in the gonads.

TABLE 1.—Summary of estimated population doses of radiation to the gonads expressed as percentages of natural background. (This table is reproduced by kind permission of the Medical Research Council.)

parts of the world. He also receives radiation from cosmic sources which is particulate and of high energy. Finally, from natural sources he ingests a number of unstable isotopes of common elements in foodstuffs such as

potassium^{40}, carbon ^{14}, and small amounts of radium ^{226}. These last must be of small importance in contributing to gonad dose.

Man-made sources of radiation are increasingly various, the most important being diagnostic and therapeutic procedures in medicine, particularly x-rays. There are also those from industrial use of x-rays, in the handling or use of radioactive materials in science and industry, and so on.

Finally, there is the fall-out from test explosions of nuclear weapons. Except for those in the immediate vicinity there is no direct irradiation by electro-magnetic waves or by neutron streams, but radioactive isotopes are formed in various ways and escape into the higher atmospheres. The fission products themselves, isotopes induced in the casing of the bomb and isotopes induced in elements in the atmosphere by intense neutron streams immediately round the explosion all reach the atmosphere. Most of these are very short-lived and therefore of little practical importance. Some, however, have long half-lives and eventually reach the earth. Their importance thereafter lies in the amount of penetrating radiation they produce, in how far they are ingested in foodstuffs and finally, in how far those ingested are specifically concentrated or retained in an organ or tissue. So far as genetic effect is concerned we can ignore as of relatively very small importance all effects except gamma-emitting isotopes and cæsium^{137}.

The relative contribution of specified natural and man-made sources is set out in table I.

DOSAGE OF SIGNIFICANCE IN GENETICS

Clearly, to induce changes in germ cells ionizing radiations must reach the gonads, and if the mutations are to be handed on to future generations they must be induced before the end of child-bearing age. In most calculations a period of exposure of thirty years from birth is used and a 'genetically significant dose' is arrived at, taking into account internal and external exposures, allowing for shielding factor by sexes and so on.

RELATIONSHIP BETWEEN DOSAGE AND MUTATIONS PRODUCED

Here we have no guidance directly from man and such information as is available for animals suggests that there are considerable variations in sensitivity at the different loci studied: even although loci studied tend to be of one type—those at which mutations determining specific visible traits are induced.

In the absence of any meaningful estimate of a dose/mutation induced relationship the 'doubling the mutation rate dose' has been introduced. This assumes an average rate per locus and has the advantage that it enables some rather hazardous estimates to be made of the effects on single loci at which harmful mutations occur in terms of numbers of persons consequently affected by such traits in a population.

In most parts of the world the naturally occurring radiation seems to determine about three rœntgens over a thirty-year period to the gonads. If all spontaneous mutations were so caused then the doubling dose would also be three rœntgens. On the analogy of animal work this figure is much

too low and the very scanty information which emerges from study of the first generation offspring of those exposed to the bombs in Japan suggests that the very lowest limit of the doubling dose would be ten rœntgens (Neel and Schull, 1956). The Medical Research Council Report suggests that it probably lies within a range of 30 to 80 rœntgens and the U.N. Scientific Committee gives the wider range of 10 to 100 rœntgens. The present increments that the population is receiving from man-made sources (table I) are therefore likely to be far less than a doubling dose.

The reader will now realize how impossible it is in our present state of knowledge to estimate with any confidence the amount of damage which might result from anticipated increments in radiation exposure. Indeed it is only possible to make rough estimates of the effects on one category of loci: those at which single harmful mutations arise and where the trait frequency is a direct product of the mutation rate and of the degree of selection against the trait bearer (see p. 564). Even such an estimate can only be expressed with any confidence in terms of doubling dose and we can only estimate that within wide limits. It is not surprising, however, that when this last group constitute more than 1 per cent. of all births many scientists have expressed alarm. Looked at in terms of births per annum in the whole world the resultant figures are imposing.

In short, it is not possible to estimate genetical damage from a given amount of exposure or to express it in meaningful terms. It is possible to speculate along certain lines but perhaps this has been done too often already.

SUMMARY AND CONCLUSIONS

After examining the evidence, although most of it is incomplete, we must conclude that all ionizing radiations increase mutation and that the over-all effect cannot be conceived of as other than harmful. It follows that every possible step must be taken to reduce the exposure of individuals and groups to unnecessary exposure. As, in our own society, diagnostic radiology contributes much more man-made exposure than any other to the population under thirty years of age, medical men have a peculiar responsibility. Clearly the interests of the individuals who require diagnostic x-rays are to some extent in conflict with the interests of future generations—of individuals whose ancestors they may be, but who have hundreds or thousands of other ancestors including the reader.

Further, such numerical estimates as have been made have seldom, if ever, specified the pre-existing frequency of developmental anomalies and have tended to ignore the important buffering mechanisms mentioned (pp. 563, 566). Even without conflict with the interests of patients, however, apparatus can be designed, maintained and used so that the minimum of stray radiation reaches the gonads, and gonads can often be shielded. It is difficult to conceive that any experienced doctor would maintain that the number of exposures per person could not be reduced by avoiding repeat exposures when past records can be obtained, and by restricting the use of

x-rays more firmly to occasions when they are really essential to the patient's interest.

The x-ray diagnostic contribution is much more relevant to future generations than to the present one, as individual dosages are small but many people—eventually the whole population—are exposed. For somatic effects there may well be a threshold except possibly in the case of exposures of the fœtus *in utero* (Stewart *et al.*, 1958). Other important points are that the ages of patients exposed are important in the context of subsequent childbearing and that a few procedures requiring abdominal fluoroscopy or repeated radiography contribute a very considerable proportion of the total exposure received by the population.

In the relationships of doctor and patient or family there can seldom be any radiation genetics problems. The chances that the immediate offspring of any individual exposed even to therapeutic doses, far less diagnostic exposures, would be affected in any way are extremely small and can be ignored, but the risk of harmful mutations having been induced is there and for future generations the sum of these risks is such that some individuals may eventually have to pay a price for any increased exposure to radiation.

References

Allison, A. C. (1954): *Ann. hum. Genet.*, **19**, 39.

Carter, T. C. (1958): *Brit. J. Radiol.*, **31** (in the press).

Cheeseman, E. A., Kilpatrick, J. S., Stevenson, A. C., and Smith, C. A. B. (1958): *Ann. hum. Genet.*, **22**, 235.

Ford, E. B. (1945): *Biol. Rev.*, **20**, 73.

Haldane, J. B. S. (1956): *Ann. hum. Genet.*, **20**, 344.

Lerner, I. M. (1954): 'Genetic Homeostasis', Edinburgh.

Medical Research Council (1956): 'The Hazards to Man of Nuclear and Allied Radiations', H.M. Stationery Office, London.

Muller, H. J. (1956): *Brookhaven Symp. Biol.*, **8**, 126.

National Academy of Sciences and National Research Council (1956): 'The Biological Effects of Atomic Radiation', Washington, D.C.

Neel, J. V. (1958): *Amer. J. hum. Genet.* (In the press).

——, and Schull, W. J. (1956): In 'The Effect of Exposure to the Atomic Bombs on Pregnancy Termination in Hiroshima and Nagasaki', Nat. Acad. Science, Nat. Research Council, Washington, D.C.

Newcombe, H. B. (1952): *J. cell comp. Physiol.*, **39**, Suppl. **I**, 13.

Penrose, L. S. (1957): In 'Effect of Radiation on Human Heredity', H.M. Stationery Office, London.

Russell, W. L., and Kelly, E. M. (1958): *Science*, **127**, 1062.

Stevenson A. C. (1957a): U.N. Document A/AC.82/G/R. 104.

—— (1957b): In 'Effect of Radiation on Human Heredity', H.M. Stationery Office, London.

—— (1958): 'Proceedings of the First International Congress on Radiation Research'. (In the press).

Stewart, A., Webb, J., Giles, D., and Hewitt, D. (1956): *Lancet*, **ii**, 447.

——, ——, and Hewitt, D. (1958): *Brit. med. J.*, **i**, 1495.

Turpin, R., and Lejeune, R., and Rethore, M.-O. (1956): *Acta genet.* (*Basel*), **6**, 204.

United Nations General Assembly (1958): 'Report of the United Nations Scientific Committee on the Effects of Atomic Radiation', General Assembly, Thirteenth Session, Supplement No. 17 (A/3838), New York.

Waddington, C. H. (1940): 'Organisms and Genes', London.

World Health Organization (1957): 'Effect of Radiation on Human Heredity' H.M. Stationery Office, London.

RADIATION FROM NATURAL SOURCES

By F. W. SPIERS, D.Sc.

Professor of Medical Physics, University of Leeds

INCREASING interest has centred in recent years on the dose of ionizing radiation which is received continually and inevitably by human beings from natural sources in their environment. Although the presence of these atomic radiations was only recognized at the beginning of this century, they have existed at all times since the formation of the earth's crust. One consequence, however, of the modern use of x-rays and atomic radiations in medicine, science and technology is that some populations are now exposed to doses of radiation additional to those received naturally. Ionizing radiation, so called because its primary act is to 'ionize' an atom by removing an electron from it, is known to produce chemical action, followed by biological change in any irradiated living tissue. Some of the consequences of exposure to comparatively large doses of radiation are known, and in man these include damage to the hands of pioneer radiologists and the development of cancer of the bone in some of the early radium luminizers; in the animal world, they include the induction of gene mutations in irradiated fruit flies and in small mammals. It must be emphasized, however, that these doses, causally associated with the development of cancer, are very large compared with the small slowly accumulated dose received by individuals from environmental or 'background' radiation. For this reason it is impossible in the present state of knowledge to deduce quantitatively the role of the background radiation in biological evolution or to assess with any certainty the effect of an increase in its intensity. It is all the more important at this time to know the level and range of the intensities of background radiations and to relate to them the increments from man-made sources.

EXTERNAL AND INTERNAL SOURCES

The radiation dose received naturally by the human body arises partly from external sources, which include terrestrial radioactivity and cosmic rays, and partly from internal radioactivity acquired by the body from air, food and water. In many circumstances the greater part of the external radiation is contributed by the local gamma radiation arising from traces of radioactivity in the earth's surface and in building materials. Indoors this component of the dose depends upon the construction of the building: it is low where wood is used, higher in buildings of brick or granite and highest where, for example in some parts of Sweden and India, unusually radio-

active shales or sand have been used as building materials. Usually the local gamma radiation is less out-of-doors than indoors, being very low over chalk and high over granite, but again the relationship can vary considerably according to the local terrain and the nature of the dwellings. The dose contributed by cosmic radiation, originating outside the earth, is usually less than the local gamma ray dose but the radiation is so penetrating that there is little difference between the dose indoors and that out-of-doors. Great thicknesses of rock or water are needed to reduce the cosmic ray intensity to small proportions; the cosmic ray dose-rate in the basement of a multi-storey building, for example, would only be some 20 to 30 per cent. less than out-of-doors; it is probably less than one per cent. of the surface value in the deeper parts of the London Underground transport system. The radiation dose to the soft tissues of the body arises from internal sources: almost entirely from potassium which is present in tissues and which contains a very small proportion of a naturally occurring radioactive isotope, potassium^{40}. In bone, part of the dose is contributed by short-range radiations (alpha rays) emitted by traces of radium and thorium which follow calcium in the food chain. In all tissues very small additional doses arise from a naturally occurring radioactive carbon, carbon^{14}, and probably also from the radon and thoron which are radioactive gaseous products of the elements radium and thorium.

The possible long-term consequences of radiation in which scientific interest has chiefly centred are genetic effects and the induction of cancer. Induced changes in the structure of a gene, leading to changes in inherited characteristics can follow irradiation of the gonads, but estimates of the magnitude of such effects can only be inferred from information gained with insects and small animals. The possible carcinogenic effects so far considered have been chiefly those in bone and bone marrow, although radiation-induced cancer has long been recognized clinically in the skin. In relation to long-term effects the tissues considered are therefore those of the gonads and bone. The dose received by various body organs varies with depth within the body because overlying tissues partly shield internal organs from the local gamma radiation. On the average, the local gamma ray dose received by human gonads is a little less than two-thirds of that recorded by an unshielded measuring instrument, and it is likely that bone and bone marrow are shielded to about the same extent.

GEOGRAPHICAL VARIATIONS

A representative value for the average dose inevitably received by human gonads in this country is considered to be about 100 millirœntgen (mr) per year, of which 28 mr is contributed by cosmic rays, 20 mr by body potassium, some 48 mr by local gamma rays and the remainder by the other small sources mentioned earlier. (The millirœntgen is one-thousandth of one rœntgen, a unit of dose, commonly used in radiology, which is

equivalent to a release of approximately 100 ergs of energy per gramme of tissue.) At sea level and at moderate altitudes variation in the total background dose is provided mainly by the local gamma-ray contribution, but, because the gonads are partly shielded by overlying tissues, the variation in gonad dose from one locality to another is less marked than might at first be supposed. Thus, in going from a limestone district where the external gamma ray dose-rates are in the range 20 to 40 mr per year to a granite area where the local gamma ray dose-rates can average 85 to 105 mr/year, the total annual gonad dose would rise from about 75 mr in the former region to about 110 mr in the latter. Although greater intensities of gamma radiation can be found in very localized areas, it would appear that great differences in the average gonadal dose are not to be expected in areas of this country where most of the population lives. On the other hand, in some types of Swedish house the average dose to the gonads may be 50 per cent. higher than the values given for the granite areas in this country and in some coastal areas of India the figure may be as much as five times as great, due to a local gamma-ray background roughly ten times that in Britain. Lastly the cosmic-ray intensity increases with altitude and at 15,000 feet (4,750 metres) the cosmic-ray dose is about six times as great as at sea level, giving a total gonadal dose of about 230 mr per year.

FOOD AND WATER

Bone is irradiated, like any other tissue, by cosmic rays and gamma rays external to the body. There is less potassium present in bone than in soft tissues but loss of internal irradiation on this account is more than made up by short-range alpha rays from traces of radium and thorium which become incorporated in the mineral parts of the bone. The amounts of radium and thorium in human bone are known approximately and are known to vary somewhat from one locality to another. The background dose to bone is almost certainly greater than that to other tissues in the body but the amount cannot be given with any accuracy, beyond estimating that it could be up to 50 per cent. greater. Radium and thorium reach the bone via the food chain and only a part of this is contributed by the drinking water. It has also been shown that most city waters contain very little of any radioactivity present in the 'raw' unfiltered water and it appears unlikely that the background dose-rates to body tissues of the inhabitants of spas differ much from the average for other areas. The average dose to bone marrow is not appreciably influenced by the short-range alpha radiation from the radioactivity in the bone mineral and is, to a first approximation, of the same order as that to the gonads.

FUTURE PROSPECTS

In modern communities the average radiation dose to the population is undoubtedly increased by the medical use of x-rays and by other man-made

radiation sources, including the explosions of test nuclear weapons. It is thought that in this country the average gonadal dose may be increased by about 25 per cent. above that from the natural background and that, of this amount, 22 per cent. is contributed by the use of x-rays for the diagnosis and relief or cure of human ailments. The pick-up of radiocæsium from bomb fall-out is contributing an addition of approximately one per cent. to the background dose-rate to the gonads and the present level of strontium^{90} in bone is adding two to three per cent. to what is estimated to be the background dose to bone. The 'nominal' background dose-rate of 10 mr per year produces a dose of 6r in 60 years and it may be justifiably asked what significance this dose, or any addition to it, may have in relation to the mutation rate in man or to human morbidity.

In my opinion a quantitative answer cannot yet be given, because experience gained at higher doses (some hundreds or thousands of r) and higher dose-rates provides only an insecure basis for extrapolation to levels of dose as low as 6r spread over a lifetime. There can be no doubt that natural radiation plays a part in providing the gene mutations on which evolutionary processes work, but what fraction of the present human mutation rate can be ascribed to background radiation and what to other physical and chemical causes can only be estimated within very wide limits on the basis of animal experiments. Similarly, no geographical variation in the incidence of any disease has yet been correlated with differences in the radiation background. These and similar questions provide a challenge which many investigators in many countries are attempting to meet. The levels of natural background radiation in which populations live, the natural radioactivity in man and in food, and the biological effects of small doses of radiation are being intensively studied. When finally known, the biological role of the radiation background in which man has always lived will be a fascinating and important contribution to the knowledge on which the safe use of man-made radiations can be based.

Selected Bibliography

General:—

British Journal of Radiology (1957): 'The Measurement of Body Radioactivity', suppl. no 7.

Medical Research Council (1956) 'The Hazards to Man of Nuclear and Allied Radiations', H.M. Stationery Office, London.

Spiers, F. W. (1956): *Brit. J. Radiol.*, **29**, 409.

Observations of Local Gamma-ray Background:—

Gould, A. R. (1958): *Brit. J. Radiol.*, **31**, 168.

Hultqvist, B. (1956): *K. Svenska Vetensk. Akad. Handl.*, **6**, no. 3.

Spiers, F. W., and Griffiths, H. D. (1956): *Brit. J. Radiol.*, **29**, 175.

Vennart, J. (1957) *Ibid.*, **30**, 55.

Willey, E. J. (1958): *Ibid.*, **31**, 31.

THE HAZARDS OF DIAGNOSTIC X-RAYS

By W. M. COURT BROWN, O.B.E., M.B., D.M.R., F.F.R.

Director, Medical Research Council Group for Research on the General Effects of Radiation, Western General Hospital, Edinburgh

THE publication in 1956 of the report by the Medical Research Council on 'The Hazards to Man of Nuclear and Allied Radiations', and also the report by the United States National Academy of Sciences on 'The Biological Effects of Atomic Radiation' focused attention on the possible risk of exposure to low doses of radiation. In this respect considerable discussion has taken place since 1956 about the potential hazards of the use of x-rays for medical diagnosis. To set this particular subject in its correct perspective two basic problems must be considered: (i) the doses received from diagnostic x-ray procedures and the frequency of such procedures, (ii) the extent to which available knowledge supports the suggestion that low levels of dose may be hazardous.

RADIATION DOSAGE AND DIAGNOSTIC RADIOLOGY

It is customary to contrast the radiation exposure from such artificial radiation sources as diagnostic x-ray tubes with the dose received from natural background radiation. In Britain the dose to the gonads per person from this latter source is on average about 0.1r (100 millirœntgens) a year. The radiation dose to the gonads from artificial sources is usually expressed in the form of an annual dose averaged over the whole of a given population even though, within the year, only a fraction of the population is directly irradiated. The dose is stated in this way because the most important genetic hazard of irradiation is the production of recessive mutations in the directly irradiated section of the population; through the process of mating, which for sake of argument may be regarded essentially as randomized, these recessive mutations become distributed throughout the whole population. Thus the hazard to the whole population is measured by averaging the gonad doses received by the irradiated section over the total numbers at risk. An estimate made in 1956 suggested that in England and Wales this dose was at least 22 per cent. of the dose received from natural sources (Osborne and Smith, 1956), and in making this estimate the authors weighted their calculations by the probability of reproduction as a function of age. In the same year the comparable dose in the United States was said to be about 70 per cent. of the background dose, but it is generally believed that both estimates, and particularly the British one, fell short of the real values. A more recent estimate from Australia (Martin, 1957) gives a value of about

119 per cent. of background radiation, and it is possible that, in technically highly developed countries, more comprehensive surveys will yield estimates of between 100 per cent. and 150 per cent. of the dose to the gonads from natural background radiation.

The number of x-ray examinations carried out in any one country in a given year is extremely large. Osborne and Smith (1956) estimated that

Examination	Male	Female
Head	0.8	0.2
Teeth	4.75	0.8
Chest (large film)	0.36	0.07
Chest (M.M.R.)	0.25	0.15
Barium meal	20	9
Barium enema	40	20
Cholecystogram	69	200
Pyelography	486	1,290
Pelvis	1,100	210
Hip-joint	710	210
Sacro-iliac joint	129	713
Leg and foot	3.5	0.6
Pelvimetry*	0	1,280

*2,680 to the fœtus.

TABLE 1.—Gonad doses received per radiological examination (in millirœntgens) in England and Wales (adapted from Osborne and Smith, 1956).

between 17 and 18 million examinations were made in England and Wales during 1954. Data for other countries have been summarized in a report to the United Nations scientific committee on 'The Effects of Atomic Radiation' from the international commissions on radiological protection and on radiological units and measurements (1957). For the population of the United States up to the age of 30 years it is estimated that an average of 0.21 radiographic and 0.06 fluoroscopic examination is made per year per person (excluding mass miniature radiography and dental examinations). For Denmark the comparable estimate, combining radiography and fluoroscopy, is 0.23 examination, and in Sweden in hospital practice alone, excluding sanatoria and both mass miniature radiography and dental examinations, an estimate of 0.23 examination per person per year has also been made.

Much work has been done to investigate the frequency with which different anatomical sites are exposed and to estimate the gonad dose in either sex from the exposure of any given site. Thus, in England and Wales some 12 to 13 per cent. of the examinations are of the chest (excluding mass miniature radiography), whilst between 2 and 3 per cent. are barium examinations of the gastro-intestinal tract. Of the varied forms of exposure some six or seven types of examination (about 10 per cent. of all types) contribute approximately 85 per cent. of the gonad dose. A representative group of types of examination and their contributed gonad doses are shown in table 1.

So far as the red bone marrow is concerned any exposure of the trunk must

irradiate this tissue, and a special problem that has been raised is that of the possible risk to the developing fœtus of abdominal x-ray examinations, particularly pelvimetry, carried out on the mother (Stewart *et al.*, 1956, 1958). Whilst the results of the survey may be regarded as still equivocal they do focus attention on the frequency of radiographic examination of pregnant women. Estimates from several countries suggest that pelvimetry may contribute between 0.1 and 1 per cent. of all examinations, and Osborne and Smith (1956) suggested that at least 26,000 pelvimetries are performed annually in England and Wales, together with about 86,000 other obstetrical examinations.

In conclusion, therefore, it is probably fair to state that in technically highly developed communities the annual gonad dose averaged over the whole population will be as much as, and even in excess of, the dose from natural background sources. It is reasonable, also, to assume a steady increase in the number of x-ray examinations and at present, in spite of technical improvements tending to reduce the gonad dose per examination, the over-all level of this dose is probably increasing from year to year. There are no published data concerning the doses to other tissues, but these must on the whole increase with the gonad dose.

RADIATION DOSAGE AND THE INCIDENCE OF HAZARDS

Two potential hazards require consideration: the production of genetic changes in the sex cells which may be transmitted to succeeding generations, and the induction of leukæmia. Other long-term effects of irradiation have been described, particularly in man the induction of other forms of cancer (tumours of the skeleton, the thyroid, the pharynx and the skin), and in animals, as well as tumour induction, a decreased expectation of life claimed to be the result of an acceleration of the process of ageing. The discussion of cancer induction will be confined to leukæmia as practically no knowledge exists of the relationship between radiation dose and the incidence of other cancers, and to date observations tend to suggest that leukæmia may be the most important individual hazard to be faced. No evidence has been found of a perceptible decrease in the expectation of life in a large group of practising radiologists (Court Brown and Doll, 1958) and there is no reason to suppose that this particular hazard has to be considered in relation to diagnostic radiology.

GENETIC EFFECTS

The lowest dose at which genetic effects have been measured is 25r, in studies on *Drosophila melanogaster*. Work at lower doses becomes extremely difficult because of the very large numbers of animals required to be observed to produce statistically significant data although to some extent this difficulty may be offset by studies on bacteria and viruses. To date it has been accepted that the direct evidence from animals suggests a simple proportional

relationship between the dose of radiation and the incidence of mutations, and it is generally assumed that the same relationship will exist for doses of less than 25r, i.e. in the range of gonad doses received from diagnostic radiology. Satisfactory studies have yet to be made of radiation-induced genetic effects in man but, because of the universal nature of the mechanism of inheritance, it is believed that the same type of relationship will hold for man, certainly in a qualitative sense. Therefore, if it is accepted that there is a proportional relationship between radiation dose and mutation frequency, even over the lowest range of dose, it must be accepted also that all doses of radiation convey some increased probability of mutations being induced, which varies with the size of the dose, and that no safe threshold dose exists below which this does not occur. It follows that every dose of radiation received in the gonads of a person capable of conceiving a child must be deemed to increase the risk of a mutation being induced which may be passed on to the next generation. It is accepted that because man has evolved in the presence of a constant radiation background, virtually all the beneficial mutations induced by radiation will have been utilized in his evolution through the processes of natural selection. Thus for practical purposes all mutations now induced by radiations can be regarded as harmful.

It will be appreciated therefore why it is now considered that diagnostic radiology plays a part in the production of heritable disease. Estimates of the magnitude of this part are difficult to make, but Carter (1957), on the basis of a proportional dose-response relationship, has attempted to estimate the increased numbers of people in England and Wales who will carry various genetic handicaps, including mental illness, mental deficiency, diabetes, blindness, deaf mutism, and the like, if irradiation from diagnostic radiology is continued at the present rate until genetic equilibrium is established. The estimate is approximately 56,000 people, of whom about 15,000 will be sufferers from mental illness or mental deficiency. Quite apart from any other consideration the care and treatment of these people would impose a considerable financial load upon the community. There is thus a cogent argument for the reduction, so far as is possible, of the gonad dose from diagnostic radiology.

THE INDUCTION OF LEUKÆMIA

Direct observations on the incidence of leukæmia in man have not been made for a dose of less than about 100r averaged over the total red marrow (Court Brown and Doll, 1957). It has been postulated that below this level of dose there may exist a proportional relationship between radiation dose and leukæmia induction: i.e. leukæmia may be the outcome of a simple mutation in a somatic cell. This postulate remains controversial and a number of authorities believe that it is possible to suffer a certain amount of radiation exposure without incurring an increased risk of developing leukæmia, and that the basic change, if it be in the genetical mechanism of the cell, is some-

thing more complex than a simple mutation. It will therefore be appreciated that, whilst there is widespread acceptance of the assumption that all doses to the sex glands are potentially harmful, it is not permissible in considering the induction of leukæmia to do more than propose alternative assessments of the risk. It is unfortunate that murine leukæmia, the type so widely investigated in animal research, is unconvincing as a suitable model of human leukæmia. Examination of the available human data, however, would suggest that if a threshold dose must be exceeded before an increased risk is run of developing leukæmia, then it would be surprising if this dose exceeded a maximum dose of about 50r in the bone marrow.

There is one important point to make about the conditions of exposure in diagnostic radiology in relation to leukæmogenesis, and it is that the exposures are given at a high dose-rate. All the described cases of human leukæmia, which have probably been induced by radiation, have followed exposures at high dose-rates, the rates ranging from about 20r per minute up to the extremely high rates during the explosion of a nuclear weapon. In contrast, the dose-rate from natural background radiation is of the order of 2×10^{-6}r per minute, strikingly different from a rate of about 50 to 100r per minute which is usual in diagnostic radiology. If the induction of leukæmia were of the nature of a simple gene mutation the incidence of the disease would be independent of dose-rate but, if a more complex genetical disturbance is involved, requiring for example the occurrence of multiple chromosome breaks, radiobiological studies indicate that leukæmia would be more likely to follow exposure at higher dose-rates than at lower ones. If this were the case then in theory there would exist a threshold dose, but in practice this dose could be so low as to be within the dose-range of diagnostic radiology.

Whatever the final resolution may be of the controversy regarding the mechanism of radiation leukæmogenesis, it is desirable in our present state of uncertainty to avoid unnecessary irradiation of the red bone marrow.

CONCLUSIONS

It is not sufficient simply to describe the potential hazards of medical radiology without taking into account the undoubtedly great benefits that accrue from this form of diagnosis. These are such that clearly no-one would be foolish enough to feel that in the long run their value was outweighed by the possible hazards. It is realized that a certain degree of hazard is acceptable, in as much as a certain degree of risk is acceptable, and indeed inevitable, in the performance of such a procedure as a laparotomy. There is every reason, however, while accepting that some risk is inevitable, for reducing this risk so far as is possible. Fortunately, a number of measures can be taken which will greatly reduce the potential risk, and in this respect attention is drawn to the work of Ardran and his colleagues.

Ardran (1956) has pointed out how it is often overlooked that for a long

time radiologists have been concerned with problems of dose reduction, and he draws attention to the remarkable degree of reduction that can be achieved through such technical advances as filtration of the primary beam, its limitation by suitable cones and diaphragms, and the introduction of high-speed films. Thus, in the Nuffield Institute for Medical Research the skin dose per film, when examining an area of the average human abdomen 5 inches (12.5 cm.) in diameter, was progressively reduced from 1.4r in 1938 to 0.13r in 1953. A further dramatic reduction to 0.012r was obtained by the use of an image intensifier and 35-millimetre film. Such measures, together with the use of equipment free from the leakage of stray radiation, cannot but produce an appreciable reduction of dose to the gonads and to the bone marrow. A further important measure to take, which could be universally applied, would be the use of protective shielding of the external male genitalia and of the lower abdomen in women. Ardran and Kemp (1957) have devised such equipment for the protection of the male genitalia, and have suggested that, provided the primary beam is reduced to a minimum, the use of this should reduce the gonad dose to the population by about 25 per cent. Finally, it is an undoubted fact that much unnecessary duplication of films occurs, and if all members of the medical profession cooperated in reducing the number of x-ray exposures to the minimum necessary for the adequate management of the patient, a further appreciable reduction would occur in the doses to such important target tissues as the testes, the ovaries and the bone marrow. The use of all these measures would go far towards reducing the risks to within acceptable limits and at the same time provide latitude for further expansion in the use of medical diagnostic radiology.

References

Ardran, G. M. (1956): *Brit. J. Radiol.*, **29,** 266.

——, and Kemp, F. H. (1957): *Ibid.*, **30,** 280.

Brown, W. M. Court, and Doll, R. (1957): *Spec. Rep. Ser. med. Res. Coun. (London)*, No. 295.

——, —— (1958): *Brit. med. J.*, **ii,** 181.

Carter, T. C. (1957): *Brit. J. Radiol.*, **30,** 641.

International Commissions on Radiological Protection and on Radiological Units and Measurements (1957): *Phys. in Med. Biol.*, **2,** 107.

Martin, J. H. (1957): *Proc. Coll. Radiol. Aust.*, **1,** 103.

Medical Research Council (1956): 'The Hazards to Man of Nuclear and Allied Radiations', H.M. Stationery Office, London.

National Academy of Sciences and National Research Council (1956): 'The Biological Effects of Atomic Radiation', Washington, D.C.

Osborne, S. B., and Smith, E. E. (1956): *Lancet*, **i,** 949.

Stewart, A., Webb, J., Giles, D., and Hewitt, D. (1956): *Ibid.*, **ii,** 447.

——, ——, and Hewitt, D. (1958): *Brit. med. J.*, **i,** 1495.

STRONTIUM^{90} AND HUMAN FOOD

By R. SCOTT RUSSELL, M.A., Ph.D.
Agricultural Research Council Radiobiological Laboratory, Grove, Wantage, Berks.

Although strontium and calcium do not move at identical rates through biological systems their behaviour is sufficiently similar for the fate of strontium^{90} to be largely inferred from a knowledge of the metabolism of calcium. In the United Kingdom, dairy produce provides over 50 per cent. of the dietary calcium (Ministry of Agriculture, Fisheries and Food, 1957), and the data now available suggest that rather more than 50 per cent. of the strontium^{90} in the average diet is present in dairy produce (Bryant *et al.*, 1958). The level of strontium^{90} in milk is thus a principal question of concern.

THE FACTORS INVOLVED

In considering the factors which affect the level of strontium^{90} in milk and in other foods, it is necessary to examine the individual steps in the food chains through which it passes into diet (fig. 1). Strontium^{90} which falls on the surface of agricultural land will lodge to varying extents on the foliage or on the stems of plants, or on the soil. An interchange of strontium^{90} occurs between the plant and the soil. A fraction of the strontium^{90} originally deposited on plants will be removed by rain (Middleton, 1958), or by the death of leaves. Strontium^{90} may simultaneously be absorbed by roots from the soil. The contaminated plants may either be consumed by man or alternatively the dairy cow may intervene transferring the strontium^{90} to milk. Apart from the food chains illustrated in fig. 1, the possibility exists that strontium^{90} may reach man also through water, either in drinking water or through edible fish. Neither route appears at the present time to be as important as a dry land food chain, and they are therefore not further considered in this article.

It is important to distinguish between the 'direct' contamination of vegetation with strontium^{90} which has been deposited on it, and contamination due to absorption from the soil. Because the leaves of plants can intercept a significant part of the deposition, perhaps 25 per cent., 'direct' contamination would be the cause of immediate concern if a large accidental release were to occur. The absorption of strontium from soil is a relatively slow process but, since strontium^{90} is neither leached from the soil, nor fixed in forms in which it is inaccessible to plants to a significant extent, this route of entry would eventually become dominant.

For interpreting the effects of world-wide fall-out an important difference between 'direct' contamination and contamination from the soil is that the former depends upon the rate of fall-out during the period of growth of crops, whereas the extent of entry from the soil is related to the cumulative

deposition. With the passage of time the cumulative total will increase in the soil relative to the annual deposition. Thus, as world-wide fall-out continues, absorption from the soil will contribute an increasing fraction of the strontium^{90} in plants.

We are still at an early stage in understanding the factors which control the contamination of vegetation, but it is already apparent that under different agricultural conditions very different relationships can exist between the level of strontium^{90} in agricultural produce and both the rate of deposition and the cumulative fall-out. This is well illustrated by the results of surveys of strontium^{90} in milk at Frome, Somerset, and in the New York area (fig. 2). In both localities fall-out has increased steadily during the period of observation. In Somerset, however, the contamination of milk has been considerably greater relative to the deposition, and it has changed with time to a considerably smaller extent. This suggests that in Somerset the extent of contamination is largely related to the mechanism dependent upon the rate of fall-out, whereas in the New York area it is more related to the cumulative deposition. Futhermore, it appears that for a given deposition the rate-dependent mechanism of entry, that is to say 'direct' contamination, leads to considerably higher levels of strontium^{90} in milk. Knowledge of the route whereby strontium^{90} enters diet is clearly essential if future trends are to be interpreted.

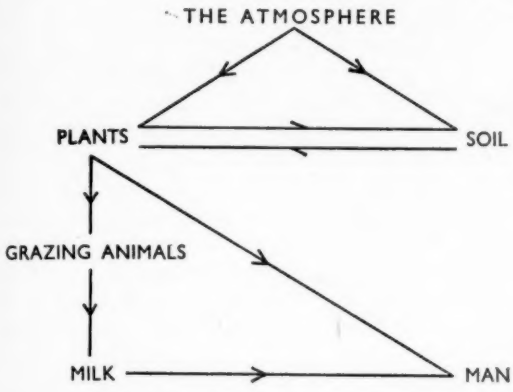


FIG. 1.—Principal food chains when strontium^{90} is deposited on agricultural land.

THE ABSORPTION OF STRONTIUM^{90} FROM SOIL

If plants are grown in simple artificial systems (for example, in solution culture) strontium is absorbed at a relatively similar rate to calcium. In soils, this simple relationship does not generally occur. There are two reasons for this. The calcium in soils exists in a wide range of physico-chemical states, and only a fraction of it (which in many soils cannot be satisfactorily measured by present methods) effectively dilutes the added strontium^{90}. Moreover, because of the slow movement of strontium^{90} in soils, it is confined largely to the upper 2 or 3 inches (5 or 7 cm.) (Eisenbud, 1957) when the soil is not disturbed. In cultivated land strontium^{90} will be distributed down to the depth of ploughing. Plant roots penetrate below these zones

to extents which vary greatly depending upon many circumstances; thus the ratio of strontium^{90} to calcium in the upper soil layers provides only limited information as to the relative concentration of the two ions throughout the region which is explored by the roots of plants.

The results of experiments so far available suggest the following general conclusions. If soils contain less than 1 g. of calcium per kg. which is in a

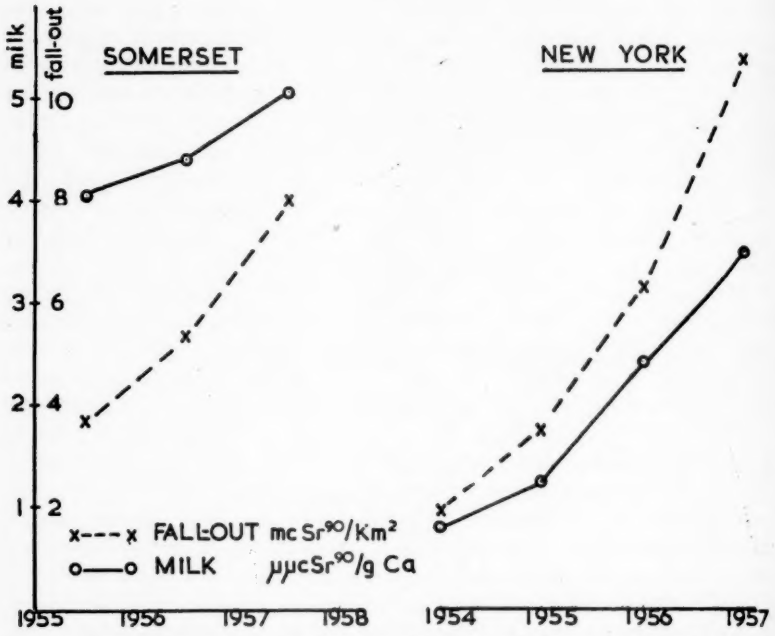


FIG. 2.—Comparison of the relationship between the deposition of strontium^{90} and the levels in milk in Somerset and New York. (Data from Bryant, *et al.* 1958; Eckelmann, *et al.* 1958; Stewart, *et al.* 1957, 1958).

readily extractable form (i.e. it can be displaced by such solutions as normal ammonium acetate) the absorption of strontium^{90} will be greater than in more calcareous soils, and the addition of lime may reduce absorption by a factor of perhaps 2 or 3 (Comar *et al.*, 1957). In assessing the general situation in the United Kingdom the effects of variations in calcium supply are, however, of relatively little importance since less than 5 per cent. of all cultivated soils contain these low levels of calcium, and when soil contains more calcium the effects of both the native soil calcium and added lime are usually relatively small. The effect of the depth of plant roots on the absorption of strontium^{90} can, however, be considerable, both between different crops and different soils. Grasses and clovers of the types grown in typical pastures absorb a considerably greater quantity of their stron-

tium^{90} and calcium from the upper soil layers, and the ratio of strontium^{90} to calcium they contain may consequently be higher by a factor of two or three than those for deeper-rooted species. Field experiments have been carried out under conditions as similar as possible to those of normal agriculture, on representative British soils in which radioactive strontium has been mixed by ploughing prior to the planting of crops (Russell *et al.*, 1957; Milburn *et al.*, 1958). From these experiments some prediction of the extent to which strontium^{90} is absorbed from the soil can be made. A comparison of these results with the observed relationship between world-wide fall-out and the contamination of vegetation shows that in permanent lowland pastures the present level of strontium^{90} is perhaps eight times greater than would be expected if strontium^{90} were absorbed from the soil. In annual crops, and edible vegetables belong to this category, the levels of strontium^{90}, however, are considerably closer to those expected as a result of absorption from the soil (Russell, 1958).

THE AERIAL CONTAMINATION OF VEGETATION

Some of the strontium^{90} which falls on agricultural land will lodge directly on the leaves of plants. When grass forms a continuous ground cover it appears that as much as 25 per cent. of the total deposition may be thus retained provided that the deposition consists of relatively small particles. If, however, large particles (40 microns or more) are deposited the direct retention by plants would be much smaller. The fate of the strontium^{90} which is not retained on leaves will depend upon the nature of the vegetation. With annual crops much of it will rapidly enter the soil, but in permanent pastures, and in this country they are particularly important being a major source of the diet of cattle, much of the strontium^{90} may lodge on the basal parts of the plants or on the surface roots which to a greater or lesser extent form a mat above the soil proper. This strontium^{90} appears to be much more accessible for absorption by plants than that which has entered the soil because it has not been diluted with soil calcium. This is believed to be the main reason why the permanent pastures at present show considerably higher ratios of strontium to calcium than annual crops (see Bryant *et al.*, 1957, 1958).

From the viewpoint of the diet of the population the importance of this situation lies in the fact that it causes the present level of contamination in milk to be greater relative to that in other foods than would otherwise be the case. Since there is a discriminatory factor in the order of 7 between strontium and calcium in their passage to milk (Comar *et al.*, 1957), the level of strontium^{90} in milk would be one-seventh of that in vegetable foods if all vegetation were equally contaminated. At the present time, however, the level in milk is similar to that in the total diet, and the ratio of strontium^{90} to calcium in green vegetables appears to be only two or three times that in milk (Bryant *et al.*, 1958).

The conclusion is therefore justified that the major part of the strontium^{90}

which is at present in vegetation or in human diet in this country has not been absorbed by plants from the soil, but has lodged on leaves or been trapped in the basal parts of plants.

VARIATIONS BETWEEN DIFFERENT PARTS OF THE UNITED KINGDOM

It is now well established that differences in the deposition of fall-out between different parts of the country depend upon variation in rainfall (Stewart *et al.*, 1957). The rainfall in the greater part of these Islands is between 25 and 75 inches (63 and 190 cm.) a year, and the variation in the total deposition of strontium^{90} consequently varies by a factor in the order of 3. Preliminary information on the levels of strontium^{90} in diet in different localities suggests a generally similar range of values (Bryant *et al.*, 1958). It has, however, been shown that in some wet hilly areas the ratios of strontium^{90} to calcium in the rather meagre hill pastures, and in the bones of sheep, are higher by a considerable factor than those in the remainder of the country (Bryant *et al.*, 1957). The explanation of this situation appears to lie in the nature of the vegetation. In these moist hill areas a 'mat' of stems, roots and peat develops on the soil surface. Strontium^{90} appears to be considerably more rapidly absorbed from the mat than from the soil. Moreover the mat traps the deposition efficiently; thus, even though fall-out has been occurring for several years, the quantity of strontium^{90} in the soil may be similar to, or less than, that in the mat. In hill areas there is therefore an unusually large reservoir of strontium^{90} in the mat to supply the relatively small quantity of vegetation which grows each year.

From the viewpoint of studying the mechanisms whereby strontium^{90} enters plants this situation is of considerable interest; to the medical practitioner, who is responsible for the health of the people, however, it is relatively unimportant. The hill areas where the situation occurs are in the main suitable only for the grazing of sheep, and from them relatively little strontium^{90} or calcium passes into human diet. If pastures are managed in such a manner that they are a productive source of grazing for cattle, the level of strontium^{90} is considerably reduced; the same, of course, applies to land in which annual crops are cultivated. It thus seems that, although very striking differences can be observed if plants of certain types from one part of the country are compared with those growing in another, the extent to which strontium^{90} enters human diet varies in a relatively similar way to the rainfall. A further factor to remember is that few, if any, people subsist on food grown in a single locality; this tends to level out differences still further.

RELATIVE EXTENT OF THE CONTAMINATION OF DIFFERENT FOOD PRODUCTS

From what has been said already it is apparent that the relative extent to which different food products are contaminated will depend upon whether

strontium^{90} has entered by direct contamination of leaves, stems or surface roots, or by absorption from the soil. In the former case milk will be the major source of hazard; thus, if strontium^{90} is released into the atmosphere in significant quantities as the result of an accident, the monitoring of milk will enable the magnitude of the immediate hazard to be assessed. The permissible level of strontium^{90} in the milk distributed to the general population must be determined by the hazard to children; not only do they derive a greater fraction of their dietary calcium from milk, but also they are more subject to radiological hazards because of their youth. It can be confidently assumed that if the level of strontium^{90} in milk is safe for children it will be unnecessary to consider other sources of immediate hazard. In fact, if milk condemned for use by children is used for cheese- or butter-making the level of contamination in these products may be considerably below the permitted level.

If, however, the deposition has occurred some time previously so that the strontium^{90} is mainly in the soil, the situation will be different. All plant species appear to absorb strontium^{90} and calcium at relatively similar rates, except in so far as the distribution of their root systems causes variations. It follows therefore that absorption from uniformly contaminated soil will cause all vegetable produce to be equally contaminated, whilst dairy produce will show a considerably lower level of contamination because of the discrimination factor against strontium in its passage from the diet of cattle to milk.

At the present time when world-wide fall-out has been occurring at a relatively steady rate for four or five years the situation is intermediate between these two extremes.

FUTURE RELATIONSHIPS BETWEEN LEVELS OF FALL-OUT AND CONTAMINATION OF HUMAN DIET

The prediction of the future is always attractive; it is also always difficult. With regard to this subject this is particularly so since information has been, as yet, gathered over such a short period of time. The results from the Somerset milk samples shown in fig. 2 indicate, however, one important fact: the levels of strontium^{90} in diet do not rise proportionately with cumulative fall-out. The reason for this is apparent from the foregoing discussions of the aerial contamination of vegetation which is largely dependent upon the rate of fall-out. The adequate interpretation of the future situation therefore depends upon precise estimates of the rate of absorption of strontium^{90} from the soil. On this subject experimental information is now beginning to accrue; in its absence long-term predictions deserve little credence.

THE MITIGATION OF HAZARD FROM STRONTIUM^{90} IN AN EMERGENCY

Our inability to halt or accelerate the rate of decay of radioactive isotopes might suggest that hazards due to the contamination of agricultural land

cannot be mitigated. Happily this is not altogether so. In the event of serious contamination a number of protective procedures would be possible. The ploughing of land, which will mix the strontium^{90} throughout the soil, tends to reduce absorption; the replanting of permanent pastures holds promise of particular benefit since the root mat in which strontium^{90} will otherwise be retained is broken up and buried in the soil. Moreover, if serious contamination were confined to limited areas the hazard to the population could be greatly modified by replacing dairy herds by store cattle, since relatively little strontium^{90} or calcium passes to man in meat.

CONCLUSIONS

The limitations of our present knowledge on this subject cannot be too strongly stressed. At the same time, a number of encouraging facts emerge. The occurrence of higher levels of strontium^{90} in poorly growing permanent pastures than elsewhere does not imply a comparably higher level in human diet. The foods which would be the major source of hazards in different circumstances have been identified, and some methods for mitigating the hazards would be available in an emergency. Furthermore, extensive surveys of radioactivity in human food are now in progress so that the situation can be kept constantly under review.

References

Bryant, F. J., Chamberlain, A. C., Morgan, A., and Spicer, G. S. (1957): Atomic Energy Research Establishment, HP/R 2353.

——, ——, Spicer, G. S., and Webb, M. S. W. (1958): *Brit. med. J.*, **ii,** 1371.

Comar, C. L., Russell, R. S., and Wasserman, R. H. (1957): *Science*, **126,** 485.

Ecklemann, W. R., Kulp, J. L., and Schulert, A. R. (1958): *Ibid.*, **127,** 266.

Eisenbud, M. (1957): 'The Nature of Radioactive Fall-Out and its Effects on Man', U.S. Congress Report, Part 1, p. 554.

Middleton, L. J. (1958): *Nature*, **181,** 1300.

Milburn, G. M., Ellis, F. B., and Russell, R. S. (1958): (In the press).

Ministry of Agriculture, Fisheries and Food (1957): 'Domestic Food Consumption and Expenditure', H.M. Stationery Office, London.

Russell, R. S. (1958): *Nature (Lond.)*, **182,** 834.

——, and Milburn, G. M. (1957): *Ibid.*, **180,** 322.

Stewart, N. G. (1958): Personal communication.

——, Osmond, R. G. D., Crooks, R. N., and Fisher, E. M. (1957): Atomic Energy Research Establishment HP/R 2354.

RADIATION HAZARDS AND PUBLIC HEALTH PREVENTIVE MEASURES

By ANDREW B. SEMPLE, V.R.D., M.D., D.P.H.

Medical Officer of Health, City and Port of Liverpool; Professor of Public Health, University of Liverpool

DURING the progress of civilization each stride forward has, in addition to the improvement in mankind's standard of living, produced as a side-issue hazards which often had serious health consequences. With the harnessing of steam power to the machine in the eighteenth century came the factory system, the grimness and frustrations of urban slumdom, and the filth, depression and disease caused by atmospheric pollution. In recent years, the discovery and development of the use of atomic energy have placed at the disposal of man the greatest source of power ever known in the world. The one aspect in which the advance to the use of atomic energy differs from previous advances is that the health hazards are to a considerable degree known now, and if we neglect to take adequate precautions, we can imperil the health and future well-being of the community to a greater extent than ever before in history.

KNOWLEDGE OF THE HAZARDS

Although some of the health dangers of ionizing radiations had been known since the beginning of the century, it was not until scientific research made possible the use of nuclear energy as a source of power and a weapon of warfare, that ionizing radiations became a general hazard as distinct from one affecting a relatively small number of people such as x-ray workers, workers with luminous paints, and some others. Furthermore, there has been a growing awareness of the dangers of ionizing radiations in the causation of certain cancers and leukæmia when these radiations were administered for therapeutic purposes.

The great advances in the use of atomic energy took place during the 1939-45 War in the course of the development of the atom bomb and were therefore of necessity shrouded in secrecy. This military use of atomic energy tends to dominate the scene and to give the impression that the whole field of nuclear power is an obscure and complex one, full of secrets and largely in the hands of experts talking an obscure jargon. This, of course, is not the case. Nuclear energy is a source of power which is going to be used and exploited more and more in the years to come, and the control of the risks from ionizing radiations must devolve upon all medical men and to a lesser extent on certain other health workers such as public health inspectors, municipal engineers and public analysts. The Medical

Research Council Report (1956) on the hazards of nuclear radiations in discussing this point states:

> 'The hazards to health are qualitatively the same, however, whether they arise from nuclear weapons or from the use of ionizing radiation for peaceful purposes. The difference is one of degree and intensity only. As with other sources of energy that man has harnessed to his service, the use of ionizing radiation necessarily entails risk; but the risk is controllable within limits that he can accept'.

In order to ensure the maximum control of the ionizing radiation risk, wide dissemination of the fundamental principles of nuclear energy is essential. Instruction on this subject should be part of the general medical curriculum—it is already included in most courses for the Diploma in Public Health. The greatest need is for training courses for medical officers of health, their staffs and other medical men in contact with this problem. Some courses have already taken place, but more are needed, and it is hoped that this matter will receive urgent consideration. At the same time it is pleasing to note that a number of Colleges of Technology throughout the country are offering courses on the peaceful uses of nuclear energy and on radiation hazards.

I am firmly of the opinion that the first essential in the control of nuclear radiation dangers is to facilitate and encourage a widespread knowledge of the subject among doctors and those responsible for environmental health.

ATMOSPHERIC CONTAMINATION

The main concern is atmospheric contamination by radioactive particulate matter from fall-out from nuclear missile explosions or from nuclear reactors. The former is still the subject of much controversy while the latter is well recognized and has been effectively controlled. Nevertheless, an accident occurred in a nuclear reactor at Windscale on October 10, 1957, which caused a considerable release of radioactive material in the immediate neighbourhood of the plant and to a lesser extent over the country generally. By October 14 there was an unprecedented amount of radioactive matter measured in the air over London. At this time, London County Council was the only local authority monitoring the atmosphere in its area for radioactivity, and with the aid of samples submitted from other local authorities was able to show the drift of the radioactive matter southwards. The importance of this observation is that it demonstrates the need for an efficient monitoring system operated by local authorities throughout the country in order to establish a baseline of environmental radioactivity so that any variation will be detected as soon as it occurs. In the event of the accidental release of any radioactivity, speed of ascertainment is the vital factor in control.

It may be argued that environmental monitoring of this kind could well be left to the Atomic Energy Authority but, whilst the Authority keeps a fairly extensive check on radioactivity in the country generally, and is

legally bound to use all possible means to prevent the release of radioactive material, it owes no particular loyalty to any local authority. Although the Atomic Energy Authority ensures that the area medical officer of health in the vicinity of its plants is informed of its activities, radioactive material may travel much farther afield. Water supplies, and food and milk supplies coming from a distance, may be contaminated. I am therefore of the opinion that every County Council and County Borough Council should maintain an efficient monitoring service dealing with atmospheric radioactivity, together with the radioactivity in water and food supplies. By this means, a precise picture of the normal amount of ionizing radiation in the environment all over the country will be built up and any increase would lead to an immediate alert. This will increase in importance over the years as wider use is made of nuclear radiations and radioactive isotopes.

IONIZING RADIATIONS IN FOOD TECHNOLOGY

Another environmental radiation danger which will require constant vigilance in the near future is the use of ionizing radiations in food technology. It has been known for some time that ionizing radiations can kill parasites such as the *Trichinella spiralis* and the cysticercus stages of tapeworms in meat carcases. Similarly many other foodstuffs can be rendered free from infesting parasites by this means. More important still, ionizing radiations have been found to act as powerful sterilizing agents, killing pathogenic and spoilage organisms and leaving the food unharmed and free from any harmful residual radioactivity. For example, liquid whole egg widely used in the bakery trade is often infected with salmonella organisms, and heat pasteurization renders this egg product unsuitable for trade purposes. Sterilization using a radioactive source is a likely solution to this problem. Obviously, if radioactive isotopes are to be used as the source of these ionizing radiations, great care must be exercised in the food factory, and a thorough final check will be required to ensure that no radioactive material is ingested by consumers of any foodstuffs treated in this way.

CONTAMINATION BY RADIO-ISOTOPES

The third environmental hazard is the contamination of municipal sewerage systems or refuse disposal arrangements with radio-isotopes or radioactive wastes. So far as the large quantities of radioactive wastes produced in nuclear reactors are concerned, the Atomic Energy Authority is responsible for their safe disposal. If this disposal involved any local authority area, no doubt the local Council would be consulted and kept fully informed of all proposals. Until a few years ago, apart from luminizing paints, the only radioactive material outside physical research establishments was the radium used by hospitals. This was carefully controlled although on rare occasions a radium needle or some similar quantity of radioactive material got mislaid and required an intensive search to find it before any

damage was done. At present the distribution of radio-isotopes in the community has already greatly increased.

Hospitals.—Radioactive isotopes of many kinds are now widely used in radiotherapy and in medical investigation. After administration some of these isotopes, such as iodine^{131}, are excreted in the urine which then possesses some radioactivity. It is therefore nceessary to ensure that any isotope waste and excreta from patients receiving internal administration of isotopes are disposed of in a safe manner. Hospitals where radio-isotopes are used are well aware of this problem and in most instances will have already conferred on safe disposal of radioactive wastes with the medical officer of health and the engineer in charge of the sewerage system. Once again it would be well to monitor at intervals the sewage systems from premises using radio-isotopes so that any radioactivity above normal would be detected and investigated.

Academic and research establishments.—Many such establishments now carry varying quantities of radioactive substances for teaching and research purposes. These include not only university departments but also technical colleges, and research laboratories in many branches of industry. Although every safety precaution is taken, there is no readily available record of all these potential radioactive sources in any given area.

Industry.—Here again there is a steadily increasing demand for radio-isotopes for various purposes in industry. Although all safety precautions are exercised in regard to the use of such substances inside the particular factory, there need be no intimation of their use to the local authority whose services the factory may be using.

It is highly desirable that there should be some form of registration of all premises (including hospitals) where radioactive substances are used. This would allow the local authority to work in cooperation with the particular establishment to ensure maximum safety.

RADIOLOGICAL HAZARDS

It is now well recognized that the excessive use of x-rays in medical investigation or treatment can be harmful, and definite efforts are being made to limit medical radiology to essential requirements, especially during pregnancy when damage may be done to the fœtus. Whilst the small doses of x-rays used in radiology may not harm the body tissues generally, any ionizing radiation may affect the gonads; therefore protective screening of the gonads is now generally used whenever possible. The checking of radiological equipment to ensure that there is no leakage of x-rays is now a general instruction to hospital boards (Code of Practice, 1957), and is no doubt being generally applied. Similarly, the radiological equipment used by dentists and in industry requires as thorough supervision. The x-ray hazard from shoe-fitting machines, both to the subjects and the employees, has been fully investigated but in my view much stricter legislative control is necessary.

THE INDIVIDUAL

In medicine until recently the dangers from ionizing radiations concerned only a few doctors and ancillary staffs working in a specialized field and there has been a tendency to leave it to the experts. The wider use of radioactive materials not only in hospitals but also in industry has changed this and it is now necessary for every doctor to be aware of the risks and the effects of ionizing radiations. These hazards are at present being considered by a government committee under the chairmanship of Lord Adrian.

For the layman the difficulty is that there is nothing to see and nothing to feel and the effects of small doses of radiation may not show themselves until after a considerable period of time. Much can be done, however, by the presentation of the facts on the hazards of ionizing radiations in simple terms and the importance of using the medical applications only when strictly necessary. Whilst the understanding of the sources and dangers from ionizing radiations may be too complex for the man in the street to understand, he has nevertheless the right to demand that he is protected from their harmful effects. In the ordinary community this is a duty which must fall on the public health service which should be trained and equipped to deal with it.

HEALTH POLICY

There is an immediate need for training in public health service on the hazards of nuclear radiations. This could possibly best be achieved by some form of short intensive residential course. In order to build up basic knowledge of the natural radiation in various parts of the country a monitoring system should be instituted by the large local authorities to provide experience, and to form a base-line from which higher levels of radioactivity could be assessed. There should also be registration of all establishments using radiactive materials in each local authority area. Such a record would be available to the hospital service, or the factory inspectorate as required, but would also be helpful to the local authority whose sewerage and other services these establishments use, in ensuring maximum safety.

Whilst much can be done for the individual to ensure his safety in the community as far as possible, there is scope for health education to alert the medical profession and the public to the dangers of too much radiation even when given for the purpose of medical or dental investigation, shoe-fitting or the like. In the present stage of our knowledge we must accept that all ionizing radiations may be harmful and everyone should avoid all unnecessary radiation.

References

Medical Research Council Report (1956): 'The Hazards to Man of Nuclear and Allied Radiations', H.M. Stationery Office, London.

'Code of Practice for the Protection of Persons Exposed to Ionizing Radiations' (1957): H.M. Stationery Office, London.

THE CONTROL OF RADIATION HAZARDS IN INDUSTRY

By ANDREW S. McLEAN, M.B., D.I.H.

Director, Health and Safety Branch, United Kingdom Atomic Energy Authority, Industrial Group

In conjunction with the International Commission on Radiological Protection, the Medical Research Council, which is the recognized authority on radiological protection in the United Kingdom, has recommended maximum permissible levels for a wide variety of conditions of exposure to radiation. Some of these levels have been derived from the evidence on the effects of radiation on human beings, and this is described in other articles in this symposium. On the other hand, many of the recommendations relating to the amounts of radioactive isotopes that may be taken into or retained by the body are based upon the results of experimental work with animals or on theoretical treatment of the problems of metabolism and tissue dosimetry. Nevertheless, there are good reasons for believing that the recommendations as a whole are both safe and realistic and they are accepted as the standard of radiological protection by British industry generally, and in particular for the control of radiation hazards in the nuclear energy industry.

PRINCIPLES OF PROTECTION

Adequate protection against over-exposure to radiation demands careful attention to well-established principles in the design of plant, laboratories and equipment. For example, penetrating radiation can be reduced to a safe level by arranging a shield of radiation-absorbing material, such as lead or concrete, between the source of radiation and the operators. In the case of a very large source such as a nuclear reactor several feet of concrete may be necessary but, in other circumstances, relatively light shields may be adequate, and with very small sources shielding may be unnecessary. To some extent, the same objective may be attained by arranging processes so that the operators spend the minimum of time in radiation areas and this principle has led to the development of methods of remote and automatic process control.

In the case of processes involving the handling of radioactive compounds, a further set of problems arises out of the need to avoid the spread of contamination and the attendant risks of inhalation and ingestion of toxic materials. To this end, it is desirable to confine such work to special areas where suitable provision can be made to contain radioactive material in enclosed systems, to ensure adequate ventilation of working areas and to maintain proper standards of cleanliness. Where these arrangements cannot be completely effective, as for example, in maintenance work on heavily

contaminated plant, contamination of skin and clothing can often be avoided if special protective clothing is used, and the risks of inhalation and ingestion can be minimized by the use of breathing apparatus.

ASSESSMENT OF DOSES

An important feature of radiation injury is the fact that none of the diseases that can be caused by over-exposure is specific to radiation. Each has a natural incidence and there is no means of distinguishing between cases which have arisen spontaneously and those induced by radiation. In the last resort therefore the proof of success of a plan of radiological protection must depend upon a statistical demonstration of a normal incidence of disease in those exposed to radiation, supplemented by detailed and complete records of the exposure of each individual. For this reason, the accurate assessment of the radiation exposure of each individual is of great importance. The levels of penetrating radiation are normally measured regularly in all work areas, as are the levels of contamination of air and of surfaces. On the basis of these measurements, steps can be taken to limit the time spent in high-radiation areas, to isolate certain types of work and to provide protective clothing and breathing apparatus. In no case, however, is it possible by these methods to obtain an accurate estimate of the degree of exposure of any particular individual, although a rough estimate can occasionally be made of the average level of exposure of a group.

EXTERNAL RADIATION

Individual doses of external radiation are normally measured by photographic methods. Ionizing radiation impinging on photographic emulsion has the same effect as light on the grains of silver bromide, and the density of fogging of the developed film is generally a good indicator of the quantity of radiation to which it has been exposed. This response is dependent, however, upon the energy of the radiation and the method is inaccurate for very high and very low energies. In practice, standard dental-size film is used for the purpose, the film being enclosed in a holder which is carried on the chest or at the waist. When exposure of the body is non-uniform, films are worn on appropriate parts of the body; for example, on headgear or on the wrists and hands. The frequency of replacement and assessment of film is determined by the nature of the work but in most routine operations which do not change in character from day to day, assessments are usually carried out once or twice a month. In general, the numbers of films used in atomic energy establishments justify the provision of local arrangements for film assessment; e.g. dark-room facilities. On the other hand, where radiation work is no more than a small incidental activity, it is preferable to make use of a centralized laboratory such as that operated by the Radiological Protection Service. Although the photographic film provides the standard method of assessment of external radiation exposure, pocket ionization chambers have been developed specifically for the measurement of individual doses of gamma radiation and these are par-

ticularly useful where the levels of radiation are liable to be high. They are expensive, however, and they are relatively insensitive to radiation of low penetrating power.

INTERNAL RADIATION

The assessment of the internal radiation dose of an individual is even more difficult than the assessment of his external radiation exposure. Of necessity, all methods of assessment are indirect and assumptions have to be made on the basis of incomplete knowledge of human metabolic processes. Added to these difficulties are formidable technical problems in the fields of chemical analysis and instrumentation which arise from the need to identify and measure minute quantities of radioactivity. The various methods can be classified broadly into two groups. First, there are many methods of measuring radioactive isotopes in biological materials such as urine and by means of which the total body content can be estimated. Many of these methods involve elaborate chemical techniques, and in every case detailed knowledge is required about the metabolism of the element in question; in particular, about the rate at which it is excreted from the body. Secondly, instruments have been developed which are capable of measuring radiation emitted by the body following the deposition of radioactive material inside it. In this case the problems of chemical analysis do not occur, nor is there the same need for detailed knowledge of metabolism. On the other hand, the measurements depend sensitively upon the distribution of radioactive material in the body and upon the degree of absorption of radioactivity by the body itself. If the radiation emitted has a very low penetrating power, it may be completely absorbed by the body tissues, so that no measurement can be obtained outside the body. In spite of much skilled effort there is still much to be done to simplify the methods and to increase their accuracy.

MEDICAL SUPERVISION

It is customary, and likely to become mandatory, for every prospective new entrant to industrial radiation work to be examined medically. The examination usually includes a chest x-ray and a blood count, along with a general clinical examination. Its aim is to ensure a good standard of general health among radiation workers and, at the same time, to avoid exposing individuals having a possible predisposition to radiation injury. For example, those with abnormally low white blood cell counts are not regarded as suitable for work of this type. In addition, each radiation worker is usually re-examined regularly but this examination is concerned primarily with the possible effects of radiation and there is a less searching general clinical examination. Four types of tissue are considered to be of particular importance from the point of view of protection against external radiation. These are the skin, gonads (with respect to impaired fertility), eyes (with respect to cataract) and blood-forming tissues. Ideally, medical supervision should be aimed at the detection of small changes in these tissues but there are many considerable difficulties. Attempts have been made to demonstrate

the effects of small amounts of radiation by minute examinations of the skin of the finger tips and the nail-bed capillaries but these have proved successful only when the dose of radiation has been considerably in excess of the maximum permissible level. Studies with experimental animals have suggested that relatively small doses of radiation are reflected in alterations in the sperm count, but this is not a practicable method of routine supervision, although it has applications in the investigation of cases of accidental heavy over-exposure. Slit-lamp examinations of the lens of the eye have been investigated as a possible means of early detection of incipient cataract but the results have not been encouraging. For many years it has been conventional in the supervision of radiation workers to examine the peripheral blood and to regard this as an index of the state of the blood-forming tissues. The total and differential white-cell counts are the main components of the examination but hæmoglobin and red-cell estimations are often included. Unfortunately, the white-cell count is subject to considerable fluctuation, varying from hour to hour with the state of the individual and his environment. In terms of single counts therefore the method has a low sensitivity as an indicator of the effects of radiation. It might be, however, that in the absence of significant single values, trends in white-cell counts over long periods would indicate prolonged exposure only a little above the maximum permissible level. Many other biological techniques have been investigated but, as yet, there is no means of detecting the effects of radiation in doses less than the maximum permissible level.

The importance of accurate records of morbidity and mortality has already been mentioned. Particular attention is given to the incidence of diseases such as leukæmia, aplastic anæmia and bone sarcoma which have been shown to have an association with radiation and to the correlation of these records with the records of radiation exposure. In general, however, the group of diseases of greatest interest has a low spontaneous incidence and, even in a relatively large industrial population, good statistics can come only from a long period of observation. The records which have been accumulated over the past ten years show no abnormal incidence of disease among workers in the British atomic energy industry.

Once radiation injury has occurred, effective therapy is seldom a practical proposition. Although a number of substances have definite protective properties when administered before radiation exposure occurs, none is effective after the event. In the absence of a specific remedy, antibiotics and blood derivatives can be used with some benefit. When certain radioactive isotopes have been absorbed into the body by inhalation or by ingestion the rate of excretion can be enhanced by the administration of substances such as zirconium citrate and sodium calciumedetate but the applications of these methods are severely limited. The whole emphasis in radiological protection must therefore be on the prevention of injury and it is for this reason that in the radiation industry the medical officer finds himself engaged in the practice of preventive medicine *par excellence*.

CIVIL DEFENCE AND ATOMIC WARFARE

By SIR ERNEST ROCK CARLING, F.R.C.S., F.R.C.P., F.F.R., LL.D.
Consultant Adviser to the Home Office and Ministry of Health
and G. R. STANBURY, B.Sc., A.R.C.S., F.Inst.P.
Senior Principal Scientific Officer, Home Office

'Suppose ten million killed. There remain forty million to be cared for'.—Major-General S. F. Irwin.

A surprise or unresisted attack by a fleet of bombers carrying thermonuclear weapons could paralyse this Island and put it out of action. The same result might be achieved by dirigible missiles. The effect would be produced partly by material destruction, partly by elimination of stored, imported or growing food supplies, and partly by biological damage from ionizing radiation. This article touches only the last factor.

SCOPE OF CIVIL DEFENCE

Civil Defence is concerned almost exclusively with the more considerable exposures, and with the preservation or provision of circumstances in which medical men may do what they can with infusions, transfusions, special feeding and antibiotics, to preserve life and restore working capacity. How far medical science and art will succeed cannot be foreseen, but the little evidence we have points to such a degree of success that every endeavour should be made to secure it.

The flash-dose of gammas and neutrons would be operative only over an area where total destruction occurs, and is therefore of minor importance for Civil Defence. In the event of a ground burst very high doses from fall-out would build up quickly and might amount to as much as 2000r in the first hour. Study has been made of the reduction by decay with time and by shelter in existing buildings; what time would elapse after detonation before fall-out reached a given site; what precautions must be observed as to keeping food and water uncontaminated; how the radiation hazard at a given point or line can be measured and anticipated; and of many other aspects of a situation that might be desperate.

With regard to dose-rate measurements, it is fortunate that a grid covering the whole country, with posts of the Observer Corps, already exists. It is an extremely close system, and when supplied with suitable instruments should be very efficient. The members of the Corps are already expert with apparatus quite as difficult to use. Moreover, through its scientific advisers, the C.D. Corps has been training scientific intelligence officers all over the country and has held exercises which have demonstrated the feasibility of the necessary reconnaissance. Those areas of the country in

which decay has reduced the menace to a degree permitting outdoor work for a specified time will be known. The exposure dose everywhere will be estimable. It will be known to be lethal in some areas, but to be less *in diminuendo* at distances from those areas, and by timed approach it will be possible to extend help to those even in the hotter regions who have sheltered, and to promote their extradition to safer parts. When such comparatively safe regions are reached medical care, including hospitalization, largely in tented provision, will begin. The tentage will probably be predominantly an Army responsibility.

THE RISK

Radiation effects of 'nominal' bombs on Japanese cities were responsible for no more than 12 to 15 per cent. of the casualties inflicted, and virtually none of these was produced beyond the range of blast and heat-flash. With the thermonuclear bomb which might be 'the major casualty-causing agent' the death-roll would extend over immense areas of the country, perhaps the whole Island, but though heavy it would be far from total. If adequately prepared for, 'radiation-induced disease will have a favourable outcome in the overwhelming majority of cases. All facts available disprove the fatalistic or pessimistic approach frequently encountered' (Gerstner, 1957). That statement takes account of all available knowledge of the effects on man of whole-body exposure and is based on the results published by the Joint Commission for study and follow-up of the victims of the bombs on Japan, supplemented by reports on 267 Marshallese and Americans exposed to fall-out from the Bikini Atoll detonation; 23 Japanese fishermen who suffered at the same time; 15 persons involved in nuclear accidents, including two reported by the Russians. There are also records of 263 cancer patients deliberately submitted to whole-body radiation. Only these 568 persons have been studied with full opportunity for assessment of the effects soon, or immediately, after the exposure. The doses received in these cases varied from no more than 50r up to 600r. Of these only one died; some were gravely, some seriously, ill, but the great majority suffered only minor or indeed trivial damage.

The Japanese cases have been under continuous observation ever since the bombing and are so still, but much more has been reported about the fatal cases and about the long duration of the severe forms of the illness, than about those who have recovered and returned to work. The recent cases have furnished information which has permitted more precise formulation of the 'acute radiation syndrome' and its phases. There is no doubt that where skilled treatment, with all the requisite resources, is at hand a majority of all those with less than the LD_{50} will survive and recover.

Because of the long latent periods there is little information on recent cases as to late effects such as leukæmia and cancer. They are not a concern of Civil Defence in total war, although their incidence will be borne in mind when deciding on direction of personnel into a radioactive area.

There are three 'types' of the acute radiation syndrome: the cerebral, the gastro-intestinal, and the hæmopoietic. For the first, the threshold dose is perhaps 2000r, for the second 500r, for the third perhaps as little as 100r. The cerebral type is almost certain to be fatal within two days; with the gastro-intestinal type such deaths as occur are likely within two or three weeks. There are unlikely to be any deaths in the range from a threshold of 100r, but if in exceptional cases there were fatalities they would occur within two months. Put in another way it may be said that of those persons who have had from 200 to 400r of gamma radiation about one-third will die; of those from 400 to 600r about one-half (LD_{50}); of those over 800r almost certainly all. These dosage figures are probably on the high side. They were calculated on the gamma component and must be lowered to account for additions by beta particles in the fall-out. A warned and prepared population should not suffer doses of anything like that magnitude, although it must not be forgotten that additional doses will be absorbed during transit out of a fall-out area. There is no doubt some difference in individual susceptibility, but therapeutic experience indicates that it is effective by not more, at most, than a factor of two.

Such round numbers must not be allowed to obscure the range over which degrees of the phenomena characteristic of each type extend symptomatically. For example, with very high dosage whilst the terminal effects will be ataxia and epileptoid convulsions, the prodromal symptoms will include the restlessness, drowsiness, listlessness and prostration which are compatible with easily survivable exposure. The fully developed intestinal syndrome, with persistent diarrhœa, bleeding from necrosed mucosa, dehydration, electrolyte imbalance, and severe infections of the mouth, pharynx, and other parts, have their milder counterpart in the early day or two of both this and the hæmopoietic form, where, too, there is nausea and some diarrhœa, but they are transient, and vomiting is rare. In this case there follows the so-called 'latent period' which may be of from one to three weeks' duration, after which chills, fever and fatigue usher in the hæmopoietic phase, with leucopenia, thrombocytopenia, purpura, hæmorrhages, and infections uncontrolled by phagocytosis or antibody reaction. If recovery is to ensue the blood-picture tends again towards normal and convalescence continues until about the end of the third month.

THE FIRST FORTY-EIGHT HOURS

It is imperative that those within an active fall-out area should remain under shelter for forty-eight hours. In this time the dose-rate decays to only 1 per cent. of that at one hour after burst. Also, partly as a result of distance, and partly of shielding, in the central and lowest part of an ordinary dwelling-house in a built-up area the dose diminishes as compared with that in the open by a factor of about 40. Forty-eight hours also gives time for the monitoring organization to obtain a reasonable estimate of the existing and future dose-rate in the area; upon these data a decision

as to conduct of operations can be based. Further advantage can be taken of the latent period. When people within the fall-out area are to be evacuated after the forty-eight-hour sheltering, the symptoms of those who have had minor or medium doses will have ameliorated so far that they will present no difficulty; those with really high doses will have deteriorated so far that the prognosis will be obvious.

Although it will be difficult to decide from symptoms at that period, how many and which of the evacuees will require hospitalization and how soon, yet if a reasonably accurate knowledge of the dosage received can be reached, then an estimate can be made on some such lines as these: of those who have had no more than 100r, 98 per cent. will have a trivial clinical course and none require hospital admission; up to 200r, although about 60 per cent. will be moderately ill, no more than 2 per cent. will be serious enough to demand bed treatment; in the 300r range about 70 per cent. will be seriously, and the rest gravely, ill; at 400r and above, all will certainly require admission.

Given the population to be evacuated from an area, it will thus be possible to give those in a reception area some idea of the numbers for whom they must endeavour to provide 'hospital' accommodation.

PROTECTION OF CIVIL DEFENCE PERSONNEL

For civil defence purposes thought must also be given to those who may have to enter a fall-out area for purposes of rescue or to deal with essential services such as a water supply. How much, in aggregate can such people be allowed to acquire? Persons so far unexposed will be of extreme importance for preserving the working life of the whole community and must not be expended even on life-saving efforts for those whose chances of recovery to the point of return to work are extremely remote. Such a dictum is anathema to medical philosophy, but is a part of the tragedy of total war.

At present it is being suggested that the wartime emergency dose for work by an individual on a given C.D. duty should be 75r although every effort would be made to keep the exposure of as many people as possible down to 25r. A decision to accept a dose of that magnitude must be based on the urgency of the occasion. In war circumstances assessment of doses is based not on the necessity which obtains in peacetime to avoid both genetic and somatic harm to individuals and to the population as a whole, but upon a comparison with concurrent dangers resulting from heat-flash and the material destruction from blast. Some help in assessing an unknown dose may be derived from the knowledge that an early and rapid fall in the numbers of leucocytes is of bad prognosis. Absence of material fall at the end of a week after exposure indicates that the dose received has been minor.

MEDICAL CARE

Fortunately the opinion of those who have recently had the care of patients whose dosage has been in the neighbourhood of 200r mixed gamma/beta radiation is that no specific treatment is needed or advisable. Bed rest,

feeding, and good nursing are all that is required. All this should be within the competence of C.D. improvised hospitals. Nevertheless, it would be idle to minimize the extreme difficulties under which medical care could be given. Evacuation or destruction of hospital buildings, shortages of staff of all grades, shortages of essential supplies, the necessity for decontamination, difficulties of selection of those for whom treatment would be likely to be successful, lack of information as to the dose actually received, these and many other deficiencies would restrict the hope of success. Further than that, there is, so far, no practical means of counteracting the effects of radiation already received, upon the human organism as a whole.

Despite a great deal of experimental work on animals, some of it promising, there is no medicament that can be relied upon to prevent or inhibit the action of radiation on the cells of human tissues. The most hopeful results have been those from the administration or transference of marrow-cells which is followed by reappearance of active cells in the marrow of the recipient.

CONCLUSION

Notwithstanding the appalling difficulty, every Authority has faced up to the situation: food and feeding; blood and blood product supplies; water-supplies; transport; communications; monitoring; evacuation of people and of resources have all been planned. When the worst possible picture has been presented to the responsible authorities it has seemed possible in every case to give a service, at least in the less affected areas.

There are grounds upon which a defeatist attitude to thermonuclear bombing can reasonably be assumed but it should be made clear that they do not include radioactivity unless there is total absence of preparation.

Selected Bibliography

Bacq, Z. M., and Alexander, P. (1955): 'Fundamentals of Radiobiology', London, pp. 344-355.

Cronkite, E. P. (1953): 'Hæmatology of Ionizing Radiations', in 'Atomic Medicine', edited by C. F. Behrens, London, pp. 119-147.

Gerstner, H. B. (1957): 'Military and Civil Defense Aspects of the Acute Radiation Syndrome in Man', School of Aviation Medicine, U.S. Air Force, Randolph Air Force Base, Texas.

Haddow, A. (editor) (1952): 'Biological Hazards of Atomic Energy', Oxford.

Home Office (1956): 'Manual of Civil Defence', vol. 1. Pamphlet no. 1 'Nuclear Weapons', H.M. Stationery Office, London.

—— (1957): 'Civil Defence Handbook No. 6. First Aid', H.M. Stationery Office, London.

Mitchell, J. S., Holmes, B. E., and Smith, C. L. (editors) (1956): 'Progress in Radiobiology', London, pp. 491-539.

Royal Naval Medical School, Alverstoke (1957): 'Notes on Atomic Energy for Medical Officers', 2nd ed., H.M. Stationery Office, London.

Selle, W. A. (1949): 'Attempts to Prevent and Counteract Effects of Ionizing Radiations by Chemical and Pharmacological Means', University of Texas, U.S. Atomic Energy Commission.

Spear, F. G. (1958): 'Radiations and their Effects on the Individual', *Civil Defence*, **10**, March and April.

U.S. Department of Defense and the U.S. Atomic Energy Commission (1950): 'Effect of Atomic Weapons', New York.

OTITIS EXTERNA IN THE TROPICS

By ROBERT AKROYD, B.M., B.Ch.
Flight Lieutenant, Royal Air Force, Singapore

Otitis externa is a complex etiological problem. There is often a high incidence of associated dermatological conditions. It may, for instance, be the localized expression of seborrhœic dermatitis, eczematous contact dermatitis, or psoriasis; or it may be neurogenic in origin associated with a simple pruritus or a localized neurodermatitis. On the other hand, it may be primarily an infective state producing an acute or chronic diffuse external otitis of bacterial nature or a chronic or recurrent otomycosis (Senturia and Alford, 1954).

ETIOLOGY

The condition is much more prevalent in hot and humid climates (McLaurin, 1954), probably because of a combination of factors which facilitate the establishment of bacterial inflammation within the ear canal in such an environment. Sebum and cerumen have been shown to exert an antibacterial and an antifungal action, due to their lipid content, which varies according to the organism involved: streptococci are very susceptible, staphylococci much less so, whilst *E. coli* and Proteus are fairly resistant (Burtenshaw, 1948; Ricketts *et al.*, 1951). The spread of sebum on the skin surface is accelerated by moisture (Jones *et al.*, 1951; Herrmann *et al.*, 1952) and consequently a humid atmosphere might diminish the protective powers of the skin. Mole (1948) and Blank (1952) have demonstrated that the stratum corneum will actually take up moisture from an environment having a high relative humidity and this may militate against another important factor in the self-sterilization of the skin, namely dryness.

In the tropics frequent swimming is commonly believed to be a predisposing factor and this also tends to leave a damp meatus as well as probably accelerating the defatting of the auditory canal. Collins (1951) considered that an accumulation of sweat in the ear passage was probably not a factor in the production of otitis externa in hot climates.

Senturia and Liebmann (1956) were able to produce a condition resembling human otitis externa in cats and it was found that neither instillation of Pseudomonas organisms, high temperature, high humidity, removal of lipids nor trauma alone would consistently lead to the characteristic inflammatory changes, but infection with Pseudomonas organisms when combined with either trauma or lipid removal was repeatedly effective. These workers believe that trauma alone without the introduction of pathogenic bacteria will not produce the disease even under conditions of high temperature and humidity. Syverton *et al.* (1946) found a high incidence of ear-picking in cases developing otitis externa and this activity obviously may lead to both trauma and bacterial contamination of the external ear. Under tropical

conditions, once the infection has been initiated the atmosphere provides a satisfactory incubator for its development.

Bacteriological studies of external otitis in hot climates have stressed the frequency with which Pseudomonas and other gram-negative organisms occur in this condition, whilst fungi have been relegated to a minor role (Syverton *et al.*, 1946; Salvin and Lewis, 1946; Singer *et al.*, 1952). In temperate climates, on the contrary, the pyogenic gram-positive cocci are often predominant (Keogh and Russell, 1956; Bihari, 1957).

SCOPE OF PRESENT INVESTIGATION

In considering the treatment of those varieties of otitis externa with a large bacterial element the nature of the infective organism must indicate the most rational therapeutic agent to be applied. The present study is particularly concerned with an assessment of the value of neomycin and hydrocortisone and of chloramphenicol when used locally in the ear.

The cases of otitis externa studied occurred in Servicemen in Singapore attending a routine daily ear clinic. Only new cases of the disease were included in the series. During the course of eleven months 133 consecutive new cases were seen but eight of these were ultimately excluded from the analysis because of incomplete documentation or treatment, leaving 125 patients (177 ears). The average duration of service in the tropics was somewhat over two years and each patient was asked the length of stay preceding the development of otitis externa. Later in the series the number of occasions on which the patient had swum in the seven or eight days before the condition developed was determined. After recording the symptomatology a speculum examination was performed and then a bacteriological swab taken. Before treatment the affected ear was completely cleaned of discharge or wax with dry cotton-wool twists.

In the first half of the series almost all the patients were treated with 0.25 per cent. neomycin ointment, together with hydrocortisone ointment applied in the form of a wick of ribbon gauze inserted deeply into the meatus. In general the wicks were repeated on alternate days but in severe cases they were changed daily at first. The neomycin ointment was used alone for the first two or three applications to obtain a maximum antibiotic effect initially, and then subsequently in an equal mixture with 1 per cent. hydrocortisone ointment. A final wick of hydrocortisone ointment alone was usually retained for two to three days.

The second half of the series was intended to compare the effectiveness of the foregoing regime of neomycin with chloramphenicol ear-drops, 10 per cent. in propylene glycol, alternate cases being allocated to each. Patients treated with the ear-drops were instructed to insert about five drops into the ear three times daily. The response to treatment was classified according to the following criteria: excellent: cured within seven or eight days; good: cured within seven to fourteen days; fair: cured within fourteen to eighteen days; poor: longer than 18 days, no improvement after ten days'

treatment or worsening of the condition despite several days' therapy.

INCIDENCE

In the year, 1957-8, 150 Servicemen reported for treatment with newly developed otitis externa. These presented from an average population of 2,500, giving a morbidity rate of 60 cases per thousand per annum; in other words, in the course of one year more than one in every twenty Servicemen developed the condition. Nelson (1945) recorded an incidence of 50 to 70 per cent. in U.S. Forces in the Pacific. Figure 1 shows the monthly incidence of the condition in relation to the mean monthly temperature and humidity. It will be seen that in this region these are remarkably constant throughout the year. Senturia (1957) demonstrated that in an environment where a high humidity persists throughout the year there is a rapid increase in the incidence of otitis externa during hotter periods.

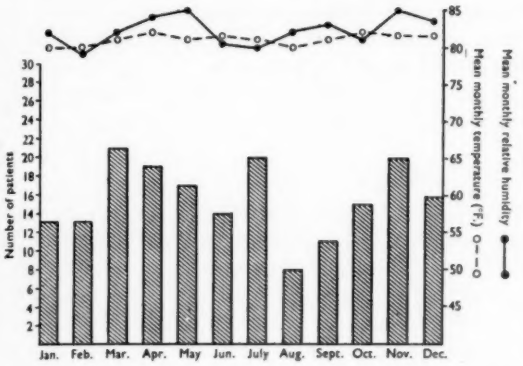

Number of patients
Mean monthly temperature (°F.) o—o
Mean monthly relative humidity
Jan. Feb. Mar. Apr. May Jun. July Aug. Sept. Oct. Nov. Dec.

FIG. 1.—Monthly incidence of external otitis in relation to mean temperature and humidity.

Of the 125 cases investigated, 52 were bilateral, 51 right-sided and 22 left-sided. In 100 cases Salvin and Lewis (1946) found that 26 were bilateral, 44 right-sided and 30 left-sided. Syverton *et al.* (1946), in a tropical series, also found that the condition was often bilateral.

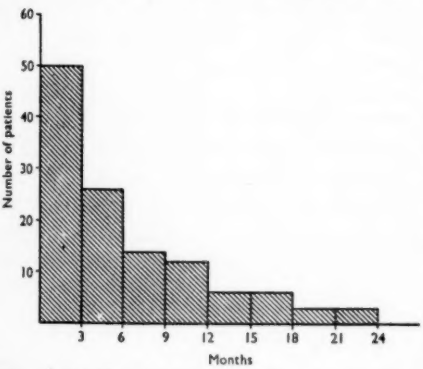


FIG. 2.—Incidence of external otitis related to the duration of residence in the tropics in 125 cases.

Figure 2 illustrates the length of time after the arrival of the patients in the tropics before otitis externa developed. It is seen that in 40 per cent. (50 out of 125 cases) the condition developed within the first three months, the numbers falling off subsequently in a smooth curve. The average age in this series was about 25 years.

Effect of swimming.—It is commonly believed among Service personnel in the tropics that swimming is a causative factor in the development of otitis externa. Syverton *et al.* (1946), however, found that only ten of their fifty patients in the Pacific gave a history of swimming in the preceding two weeks and eight of these were only occasional swimmers. In the present instance 66 otitis externa patients were compared with regard to frequency of swimming in the week preceding the illness with a similar number of healthy controls constituted of men seen for routine medical examinations. It was found that 44 (67 per cent.) patients had swum on 110 occasions. With the controls, 28 (43 per cent.) had swum on 59 occasions. Under the present conditions therefore men succumbing to the condition had definitely been swimming more often than the controls before the disease developed.

SYMPTOMATOLOGY

In a hot, humid environment acute diffuse otitis externa is common: nearly two-thirds of new patients complain of pain, with or without discharge, and nearly one-third of discharge alone. In temperate climates irritation is described as the most prominent symptom, but in the tropics this mainly occurs in chronic cases. The pain may vary from an occasional twinge to severe pain radiating in all directions around the ear causing great incapacity, usually accompanied by much meatal œdema. The pathological appearance is often determined by the type of infecting organism. The pus in *Ps. pyocyanea* cases shows a slightly bluish tinge and has a distinctive odour whilst the skin lining the external meatus presents a sodden and angry congestive appearance (Stewart, 1956). *E. coli* infections also present an unpleasant odour (Keogh and Russell, 1956) and the exudate is often small in amount and of glairy mucoid consistency (Syverton *et al.*, 1946). Proteus infections are sometimes present with thin, grey, purulent exudate and a typically foul proteolytic odour (Syverton *et al.*, 1946).

Perforation of the tympanic membrane occurred in six cases of the series. Macroscopic fungi are often observed in the meatus in tropical climates; Syverton *et al.* (1946) found them visible in seven out of 72 ears and in the present series they occurred in 10 instances. The filaments are frequently white, yellow or black in appearance and are often seen when discharge is present in the meatus but sometimes exist in a clean resolving ear, after treatment. Senturia (1957) stresses that otomycosis may result from the misuse of antibiotics applied locally to the ear.

BACTERIOLOGY

Sixty-nine swabs were taken from 54 patients in the second half of the series (table I). The results are similar to those of comprehensive studies in the tropics in stressing the importance of Pseudomonas organisms. Mixed growths occur not infrequently: in 12 cases in which pathogens were grown saprophytes were also present in five instances and other pathogens in seven, including monilia in three cases. No special attempt was made to culture

for fungi but in similar series Syverton *et al.* (1946) isolated fungi from 18 out of 72 ears and Salvin and Lewis (1946) from 16 out of 100. Those most commonly found are aspergilli, strains of actinomyces and monilia.

Organism	No. of ears	No. of patients
Staph. aureus	12	10
Ps. pyocyanea	26	22
Proteus vulgaris	6	4
E. coli	7	6
Diphtheroids only	8	8
Neisseria catarrhalis only	2	
Staph. saprophyticus only	1	
No growth	7	4
TOTALS	69	54

TABLE I.—Organisms isolated from 54 cases of otitis externa

The summary of sensitivity tests to the commoner antibiotics is shown in table II which shows the percentages of sensitive organisms. Fifteen organisms were tested against tetracycline and all were sensitive *in vitro*. Sensitivity testing for neomycin was not performed. Despite the small

Organism	Penicillin		Streptomycin		Chloramphenicol		Chlortetracycline	
	No.	%	No.	%	No.	%	No.	%
Staph. aureus	12	50	12	90	12	95	12	66
E. coli	7	0	7	86	7	100	7	14
Proteus vulgaris	6	0	6	66	6	80	6	0
Ps. pyocyanea	26	0	26	73	26	61	26	11

TABLE II.—Sensitivity of organisms to various antibiotics.

numbers of organisms tested, these findings are broadly similar to those of earlier workers studying large numbers of bacteria from routine infections (Fairbrother, *et al.*, 1951; May and Morley, 1952). Rantz and Rantz (1956), however, found that almost all the Pseudomonas strains tested were resistant except to polymyxin and that *E. coli* and Proteus as well as *Staph. aureus* have become more frequently resistant to the common antibiotics over the past few years.

TREATMENT

As already outlined, the first half of the cases were treated predominantly with neomycin-hydrocortisone ointments and the second half approximately alternately with either neomycin-hydrocortisone ointment or with chloramphenicol drops. The results of treatment are given in table III. In 16 cases parenteral penicillin was administered because of concurrent spread of inflammation to the tympanic membrane or because of severe pain and

œdema not responding to local therapy, the clinical response being excellent in two cases, good in four, fair in three and poor in seven. In two or three cases there was actually an aggravation of the condition on administering

Series	Treatment	No. of patients	No. of ears	Average time for cure	Response to treatment			
					Excellent	Good	Fair	Poor
First half	Neomycin-hydrocortisone	62	87	18 (2-56 days)	24%	44%	8%	24%
Second half	Neomycin-hydrocortisone	28	40	14 (5-38 days)	31%	42%	11%	16%
	Chloramphenicol	35	50	12 (5-28 days)	20%	60%	10%	10%

TABLE III.—Results of treatment in 125 cases of otitis externa.

systemic penicillin and occasionally the opposite ear became affected during the course of injections.

The response to treatment in relation to the bacteriology of the infection in 64 cases is summarized in table IV.

Organism	Treatment	Total no. of patients	Excellent	Good	Fair	Poor	Average time for cure
Staph. aureus	Neomycin	5	2	1	1	1	13 days
	Chloramphenicol	6	2	2	1	1	
Ps. pyocyanea	Neomycin	14	7	3	2	2	13.5 days
	Chloramphenicol	9	3	3	1	2	
Proteus vulgaris	Neomycin	2	0	2	0	0	15 days
	Chloramphenicol	4	0	4	0	0	
E. coli	Neomycin	3	2	1	0	0	13.5 days
	Chloramphenicol	4	0	1	3	0	
Saprophytes	Neomycin	5	0	4	1	0	13 days
	Chloramphenicol	5	0	3	1	1	
No growth	Neomycin	2	1	1	0	0	14 days
	Chloramphenicol	5	0	2	2	1	

TABLE IV.—Response to treatment in relation to bacteriology of infection in 64 cases of otitis externa.

Evaluation of the response to chloramphenicol in relation to the *in vitro* sensitivities showed only moderate correlation. The five cases of *Staph. aureus* and *E. coli* infections which responded poorly or only fairly well to chloramphenicol were all reported to be sensitive *in vitro*. In the case of the *Ps. pyocyanea* infections, four cases stated to be insensitive responded well to chloramphenicol and of the remaining five cases reported to be sensitive only two responded well.

This experience is in accord with that of other authors and may be due to the fact that the concentrations of antibiotic attained locally are often many times higher than those used to determine the bacterial sensitivity (Lewis and Gray, 1951) and the organisms may in fact be sensitive to the topical concentrations actually reached. In some cases the lack of correlation may be due to a change in the meatal flora produced by antibiotic treatment.

Follow up.—There is a marked tendency for otitis externa in hot humid climates to relapse. In a three-month follow up, Salvin and Lewis (1946) found a recurrence rate of 9 per cent., although these cases were usually mild. In the present series, of 72 patients (104 ears) followed for an average time of seven months, relapse occurred in 40 ears (38 per cent.) and a second relapse in 16 of these (15 per cent.). In four patients (6 ears) the condition eventually became chronic. The average time for cure of the relapses was twenty days longer than in the first attacks.

DISCUSSION

In a condition such as otitis externa, in which the etiological factors are so variable and the disease may be acute, recurrent or chronic, the only satisfactory means of assessing the comparative value of different medicaments is by controlled studies, of which few are available in the literature. The use of penicillin, streptomycin and sulphonamides locally in the ear has generally been abandoned and the application of antifungal agents routinely is now illogical. Of the other antibiotics available for local use there are sound reasons for preferring those which are not commonly given systemically, and neomycin, polymyxin and chloramphenicol are in frequent use.

The results obtained in the present study with neomycin-hydrocortisone are broadly similar to those reported by Senturia and Alford (1954) using the same compounds in cases of acute diffuse otitis externa (table V).

Series	Clinical response				No. of patients
	Excellent	Good	Fair	Poor	
Senturia and Alford, 1954	39%	42%	7%	10%	22
Present, 1957	25%	45%	10%	20%	90

TABLE V.—Comparison of results in two series of cases of otitis externa treated with neomycin-hydrocortisone ointment.

Bihari (1957), using neomycin, polymyxin and hydrocortisone in aqueous solution, obtained satisfactory results in a small series of chronic otitis externa cases after one week's treatment, but 37 per cent. (6 out of 16 cases) needed maintenance therapy for periods of up to three months. Senturia *et al.* (1954), in a controlled study of five antibiotic or chemotherapeutic agents, were impressed with the lack of superiority of one preparation over another. An attempt was also made by these workers to correlate the bacterial flora and the clinical course of the disease without success and no such evidence has been forthcoming from the present study.

There has been no uniform correlation of the bacterial flora and its sensitivities with the response to the antibiotics used in treatment.

Although the comparison between the neomycin-hydrocortisone and chloramphenicol treatments was not controlled on a statistically sound basis there would appear to be little difference in the results obtained between the two methods. Both seem to be of use in treating the new acute case as it occurs in a tropical environment.

SUMMARY

A series of 125 new cases of otitis externa (177 ears) occurring in a tropical climate among a service population is reported on.

The annual morbidity rate was 60 cases per thousand men. Evidence is presented that swimming is a predisposing factor in the development of otitis externa. *Ps. pyocyanea* occurs frequently in tropical external otitis; *Staph. aureus*, Proteus and *E. coli* are also common pathogens.

The results of treatment with neomycin-hydrocortisone ointment and chloramphenicol drops are discussed; there was a satisfactory response in approximately three-quarters of the new cases treated.

In an average follow-up period of seven months there was a relapse in 38 per cent. of the ears.

My thanks are due to the Director General of Medical Services, Royal Air Force, for permission to publish this report.

References

Bihari, J. (1957): *Brit. med. J.*, **ii**, 623.
Blank, I. H. (1952): *J. invest. Derm.*, **18**, 433.
Burtenshaw, J. M. L. (1948): In 'Modern Trends in Dermatology', edited by R. M. B. Mackenna, London.
Collins, E. G. (1951): *J. Laryng.*, **65**, 14.
Fairbrother, R. W., Martyn, G., and Parker, L. (1951): *Lancet*, **ii**, 516.
Hara, H. J. (1954): *A.M.A. Arch. Otolaryng.*, **60**, 305.
Herrmann, F., Prose, P. H., and Sulzberger, M. B. (1952): *J. invest. Derm.*, **18**, 71.
Jones, K. K., Spencer, M. C., and Sanchez, S. A. (1951): *Ibid.*, **17**, 213.
Keogh, C., and Russell, B. (1956): *Brit. med. J.*, **i**, 1068.
Lewis, R. S., and Gray, J. D. (1951): *Lancet*, **ii**, 268.
——, —— (1951): *Brit. med. J.*, **ii**, 939.
McLaurin, J. W. (1954): *J. Amer. med. Ass.*, **154**, 207.
May, J. R., and Morley, C. W. (1952): *Lancet*, **i**, 636.
Mole, R. H. (1948): *J. Physiol.*, **107**, 399.
Nelson, R. F. (1945): *Ann. Otol. (St. Louis)*, **54**, 367, quoted by Hara, H. J.
Rantz, L. A., and Rantz, H. H. (1956): *Arch. intern. Med.*, **97**, 694.
Ricketts, C. R., *et al.* (1951): *Clin. Sci.*, **10**, 89.
Salvin, S. B., and Lewis, M. L. (1946): *J. Bact.*, **51**, 495.
Senturia, B. H. (1957): *Trans. Amer. Acad. Ophthal. Otolaryng.*, **61**, 347.
——, and Alford, V. (1954): *Laryngoscope*, **64**, 834.
——, Cross, R. J., Lett, J. E., and Hardy, A. V. (1954): *Ibid.*, **64**, 1001.
——, and Liebmann, F. M. (1956): *J. invest. Derm.*, **27**, 291.
Singer, D. E., *et al.* (1952): *Otol., Rhinol., Laryngol.*, **61**, 317.
Stewart, J. P. (1956): *The Practitioner*, **177**, 698.
Syverton, J. T., *et al.* (1946): *Arch. Otolaryng. (Chicago)*, **43**, 213.

THE TREATMENT OF TRICHOMONAL VAGINITIS

By MARJORIE MURRELL, F.R.C.S., D.P.H.
Consultant in the Venereal Diseases Department
and MARY SCOTT GRAY, M.R.C.P.
Senior Hospital Medical Officer, Venereal Diseases Department, The Royal Infirmary, Edinburgh

UNTIL such time as an effective systemic trichomonacidal drug is discovered, reliance must be placed on local treatment in trichomoniasis. The fact that recurrence of infestation of the vagina is so often encountered after microscopic and cultural clearance of the trichomonads, suggests that reservoirs of infestation exist extra-vaginally.

It has been shown by sampling techniques that such sites inaccessible to local vaginal therapy exist in the female in Skene's glands (Whittington, 1957), in the urethra and in the bladder (Pattyson, 1937; Allen and Baum, 1943; Allen and Butler, 1946; Kean, 1955). Other reservoirs have been postulated such as the rectum and the cervical canal, and even the cavity of the uterine body and Fallopian tubes. The presence of *Trichomonas vaginalis* in these sites, however, has not yet been convincingly demonstrated. In the present investigation *T. vaginalis* has been recovered in the purulent discharge from Bartholin's glands.

Although the existence of distinct strains of *T. vaginalis* has been demonstrated by Lanceley (1957), using agglutination techniques, no convincing evidence has yet been produced that any of these strains develop true resistance to any particular trichomonacidal drug.

MODE OF TRANSMISSION

Undoubtedly *T. vaginalis* can be transmitted from one patient to his or her consort *in coitu*, and to this extent trichomoniasis must be considered a venereal disease. The relative frequency with which the disease is encountered in prostitutes (Greenblatt, 1945), and its frequent association with gonorrhœa in both males and females (King, Mascall and Price, 1936; Liston and Liston, 1939; Liston and Lees, 1940; Allison, 1943), lends support to this mode of transmission. Whittington (1951, 1957) found an incidence of vaginal trichomoniasis of 5.3 per cent. in 500 patients attending a birth control clinic, of 12.8 per cent. in 400 gynæcological patients, and of 21.3 per cent. in the same number of venereological patients.

In a recent survey carried out by one of us (M.S.G.), of 89 couples where the men were proven cases of non-gonococcal urethritis, the women were asked to report for examination. It was found that 50 per cent. of these women had no complaint of discharge, but on examination 38 per cent. of them were found to harbour *T. vaginalis*. Trichomonads were recovered from 64 per cent. of the total number of women examined. This was not a selected group of women and they came from various social classes: 60 per cent. of them were leading a normal, regular married life. Their ages

ranged from 20 to 40 years. It was an interesting observation that of the 71 married men 40 per cent. admitted extramarital intercourse. In contrast, only 5 per cent. of the married women admitted such conduct. In 46 per cent. of the faithful marriages trichomonads were recovered from the wife, but in only 33 per cent. of the wives whose husbands were having extramarital relationships was the organism found. A further interesting observation in this series was that, of the women in whom *T. vaginalis* was demonstrated, 65 per cent. were housewives with their own lavatories, the other 35 per cent. being those who, by virtue of their work, used outside conveniences. This lends support to the findings of Whittington (1957) that the lavatory seat is probably not instrumental in the transmission of trichomoniasis.

Menstruation, whether regular or irregular, did not appear to be a factor in the finding of the organism.

Where male contraception was practised with a sheath, 50 per cent. of the women showed trichomonads and 50 per cent. were clear; in seven cases in which female contraception was used in the form of a cap and jelly no trichomonads were demonstrated. This is of course a very small number from which to draw any conclusions, but it is possible that the contraceptive jellies used have either a trichomonastatic or trichomonacidal action.

CHOICE OF THERAPY

The local treatment of trichomoniasis must be directed at all the accessible sites of infestation and not merely at the vagina. Thus, locally effective trichomonacides must be brought into contact with the protozoa throughout the mucosal rugæ and the fornices of the vagina, the external cervical os, the female urethra and the orifices of Skene's and Bartholin's glands, and, if possible, the bladder. Ideally the male consort should be treated to prevent reinfestation. As this is virtually impossible, until such time as an effective systemic drug is produced, we advise the patient to abstain from intercourse for one month and then to have intercourse, a sheath being used, for two months. Treatment of the male has been restricted mainly to the use of a urethral jelly containing a trichomonacide, but Catterall and Nicol (1957) have found local treatment to be unsatisfactory in controlling reinfestations.

The preparations available today for local vaginal therapy in Trichomonas infestation are numerous. This fact in itself suggests that no preparation is entirely satisfactory, and this state of affairs must continue until a means is found of reaching and killing the more inaccessible organisms.

Of the drugs available for local treatment, phenylmercuric dinaphthylmethane disulphonate ('penotrane') would appear, from the results of *in vitro* tests, to be one of the more effective (Goldberg, Shapero and Wilder, 1950).

This compound is a powerful trichomonacide which was shown by Bushby, Catterall and Williamson (1955) to be the most active of fifteen drugs tested *in vitro*.

It is also a powerful antibacterial and antifungal compound, the activity of which is somewhat enhanced rather than diminished in the presence of serum. Its activity against monilia and against both gram-positive and gram-negative bacteria (Haler, 1957; Tiessen, 1957) increases its value in vaginitides of multiple etiology. The compound actively penetrates intact epithelium and for this reason should have a greater chance of reaching Skene's glands and other sites difficult of access. Previous clinical trials of 'penotrane' have confirmed its value in the treatment of trichomonal vaginitis (Platt, Seaman and Hadgraft, 1951; Kearney, 1952; Gourlay, 1955; Evers, 1957). 'Penotrane' is also protein-substantive and for this reason the trichomonacidal effect of the drug should be longer lasting since, during the intervals between local applications, effective concentrations may be maintained in the vaginal mucosa by the firm adsorption of the drug on to the cells.

SCOPE OF INVESTIGATION

One hundred and twenty-five patients attending the special clinics (V.D. and leucorrhœa) of the Royal Infirmary and the Elsie Inglis Maternity Hospital, between April 1956 and August 1957, suffering from trichomonal vaginitis have been investigated, and treated with 'penotrane' in the form of pessaries, solution, powder, jelly and vaginal tablets.

The patients at the Royal Infirmary (89) were drawn in the main from the underprivileged and morally delinquent classes and included prostitutes, Borstal and remand home cases, vagrants, and refugees. As would be expected in dealing with such clinical material, defaulters were fairly frequent. Since the patients were treated at an outpatient clinic it was impossible to know to what extent the individual patient cooperated in conscientious treatment between attendances at the clinic. Cases at the Elsie Inglis Hospital (36) were selected from the ordinary antenatal clinic because they complained of, or on examination were found to have, a purulent vaginal discharge containing *T. vaginalis*. Six of these were unmarried girls. The remaining 30 were of a better type than those attending the Royal Infirmary. They could be considered more stable, having limited intercourse with their husbands only. The majority (24) were multiparæ with homes of their own. The husbands were not investigated for *T. vaginalis*, and the frequency of reinfestation as opposed to relapse could not be estimated.

At the first attendance a careful medical and social history was taken, and a general overhaul carried out. Particular note was made regarding contacts, and the last menstrual period.

Dry films were taken from urethra, cervix and vagina to stain with Gram's stain. A swab was taken from the vaginal fornices in every case, and also from the urethra or Bartholin's glands if purulent discharge was obtained. This discharge was mixed on a slide with saline solution and safranin stain. Trichomonads were looked for and their motility recorded. Cultural methods were not used. We consider the motility of the organisms to be the most reliable guide to the severity of an infestation by a given number of trichomonads. The less motile and less robust may fail to survive culture in selective media, and, in our opinion, a diligent search of the fresh slide will invariably reveal *T. vaginalis* if it is present. We have not, however, tried the ox bile medium described by Feinberg and Whittington (1957).

The presence of coexistent gonorrhœa or monilial or bacterial vaginitis was noted.

In cases of heavy infestation, the vagina was swabbed under direct vision with an aqueous solution of the organo-mercurial under investigation. The patients were instructed to insert two of the pessaries high in the vagina every night for two weeks, but to return in one week for progress to be assessed. In most cases treatment was continued with one pessary nightly

for a further minimum period of four weeks increasing to two pessaries at menstrual periods. Only those cases with a clinical urethritis accompanied by a positive urethral smear were given local treatment of the urethra. In such cases 60 ml. of a urethral jelly containing 0.1 per cent. of the drug was introduced at the first attendance, by means of a tube fitted with a suitable nozzle. This procedure was repeated where necessary at subsequent attendances. In these cases patients were instructed to hold their urine for as long as possible after treatment. Concomitant gonorrhœa was treated concurrently.

The patients were examined again after one week, further swabs were taken, and the routine of treatment was continued. Thereafter the patients were asked to attend after two, four and eight weeks in every case, and on further occasions if, after this time, there was any doubt as to cure, and in cases of gonococcal infection when three months' observation was always advised. In non-pregnant patients the treatment with pessaries was supplemented at the clinic by the insufflation of a powder containing 0.4 per cent. of the compound, whilst in 10 patients a course of acinitrazole was given concurrently. These latter were cases complicated by urethral, Skene's or Bartholin's gland involvement. Although 'penotrane' is also available in the form of a cream this was not used in any cases in this series, since the efficient introduction of this preparation requires a degree of intelligence in the use of the applicators provided, greater than that of some of the patients included in the series. Also this treatment is not advised in pregnancy. Dry vaginal tablets were used instead of the pessaries in eight cases in which there was considered to be excessive fluor, but these were not found to be more effective than the ordinary pessaries (which are conveniently packed in sterile plastic holders of 5).

RESULTS

Of the 125 patients included in the series, 39 (32 per cent.) were found to have concurrent gonococcal infections. A frothy discharge typical of trichomonal infestation was noted in 53 cases (22 of these were also suffering from gonorrhœa). In 32 cases (28 per cent.) there was an associated clinical urethritis; of these, three patients were pregnant. Trichomonads were recovered from the urethra in 24 of these cases (22 non-pregnant and 2 pregnant). Two patients were found to have a Bartholin's abscess the purulent discharge from which yielded active *T. vaginalis*. In none of the cases was rectal infestation noted. Contraception in any form was never regular, and rarely attempted. The ages of the patients ranged from 15 years to 56 years, but one-quarter of the cases of trichomonal vaginitis, and two-fifths of the cases of gonorrhœa were in girls in their teens. Monilia were found in 21 cases (17 per cent.) in association with *T. vaginalis*: 15 of these were in patients who were pregnant. Seven patients in the series had genital warts.

In 118 cases (94 per cent.) the vagina was microscopically cleared of trichomonads at some stage during the trial. Swabs from the vagina in 72 cases (60 per cent.) were negative for Trichomonas after two weeks. Table I shows the times taken for clearance of the trichomonads from the vagina and urethra in the 118 cases cleared.

The patient who was free of infestation only after thirty-four weeks returned one week later with a heavy urethral discharge, and trichomonads were easily

Time in weeks ..	1	2	4	8	10	11	14	15	16	17	34
Number of cases ..	31	41	24	12	2	1	2	2	1	1	1

TABLE I.—Time for clearance of *T. vaginalis* in 118 cases.

demonstrated in her vagina and urethra. In the remaining seven patients (6 per cent.), the vagina was never found to be completely free of trichomonads at any time during the trial. Four of these patients failed to attend for further treatment. 44 patients (36 per cent.) defaulted at least once during observation. On the other hand, 105 cases were under observation for two months or more—the longest period of follow-up being nine months, whilst six had six weeks' observation, 10 had four weeks, and only three had two weeks in all.

Relapses or reinfestations (it is impossible to say which) occurred in 70 patients (56 per cent.) on at least one occasion: 29 (23 per cent.) of these patients had defaulted at least once. Trichomonads reappeared in the vagina or urethra, in varying numbers, at any time from two weeks to seven months after their apparent clearance.

The assessment of clinical results is notoriously difficult but it may be of value to note that the end-result so far as the patient and doctor were concerned, was classed as good in 97 cases (78 per cent.) and poor or a failure in 28 (22 per cent.) of the cases as a whole. It seemed to make no difference whether the duration of the complaint was a matter of weeks, months or years. If the group of pregnant patients (36) is compared clinically with those who were not pregnant (89), 89 per cent. of the pregnant cases were classified as good results compared with 73 per cent. of the non-pregnant. It is possible that this finding may be due to three factors: (i) the amenorrhœa of pregnancy, (ii) the relative infrequency of intercourse in the later months of pregnancy, (iii) the better social type of the average pregnant patient compared with her non-pregnant counterpart.

No benefit was observed attributable to acinitrazole in the ten patients given this drug by mouth.

Of the 21 patients in whom monilia were also recovered from the vagina, seven were free of yeasts after one week, five after two weeks, two after four weeks, four after eight weeks, and one after eleven weeks, whilst two who were pregnant went to term still infested. Four patients relapsed with a

positive monilia swab—two after eight weeks, one after twelve, and one after thirteen weeks. Monilia disappeared from the vagina in these patients following treatment with nystatin, dequalinium chloride or 'pruvagol'.

No intolerance or local sensitivity to 'penotrane' was encountered in any of the patients treated.

DISCUSSION

This study can do no more than confirm the impressions gained in many venereal disease clinics of the difficulties encountered in securing the cooperation of the patient in the treatment of a disease the consequences of which are, at the worst, only discomfort and inconvenience to the patient. Much of the benefit that might be expected to follow the time-consuming examination, treatment and advice given to such a patient may be lost by her failure to follow the advice or to return to the clinic at the proper times. Many of the patients may become reinfested during or soon after a course of treatment, or may acquire a superadded infestation while still under treatment. In this series 44 patients (36 per cent.) defaulted at least once. This figure lies midway between the 48 per cent. of Hampstein (1935) and the 22 per cent. of Stewart, Hughes, Thomas and Nixon (1957) in comparable investigations. A patient with high moral standards may feel ashamed to find herself in a position requiring attendance at a V.D. department, and often defaults as soon as her vaginal discharge ceases, thus making follow-up difficult or impossible.

It is difficult to assess the value of any form of treatment prescribed under these conditions, but a few general observations can be made. Although it is generally conceded that none of the drugs at present available for the treatment of trichomonal vaginitis is invariably successful, 'penotrane' is used by us for routine treatment as being the drug of choice because:—(1) It gives a high percentage of clinical and microscopical cures when used in the recommended dosage. (2) It is completely free from toxic reactions, either local or general in type. If there is a recurrence of symptoms it is safe to repeat the treatment without fear of sensitization having developed. (3) It is acceptable to the patient, giving rapid relief of symptoms and being easily dispensed and handled.

In treating the individual patient, it is useful that the compound is available in several different forms, i.e. pessaries, powder, solution, cream, and urethral jelly, all of which are æsthetically acceptable preparations. It is probably not as effective as nystatin or gentian violet in the treatment of monilial vaginitis, but in view of its definite antifungal activity it is of value in mixed Trichomonas/Monilia infestations.

SUMMARY AND CONCLUSIONS

The present treatment of trichomonal vaginitis is unsatisfactory. This is because trichomonacides currently available are only effective locally, and

residual foci of infestation inaccessible to the drugs occur commonly. Furthermore, local treatment by the patient herself demands active and enthusiastic cooperation. Whilst local treatment is the only form available, it is impracticable, and probably impossible, to prevent reinfestation of the female by the male. Research must therefore be encouraged to discover an effective systemic trichomonacide. Trichomonal vaginitis is more frequent in prostitutes and similar morally handicapped individuals who may fail to cooperate with treatment after clinical improvement has occurred, so that microscopical cure is difficult to achieve.

This study has served to confirm these impressions, and at the same time has shown that of the compounds available for the local treatment of trichomonal vaginitis phenylmercuric dinaphthylmethane disulphonate is, in our experience, preferable to other preparations at present available, being effective, free from toxic reactions and acceptable to the patient.

We wish to thank Dr. Robert Lees for his advice and permission to publish this investigation.

References

Allen, E., and Baum, H. C. (1943): *Amer. J. Obstet. Gynec.*, **45**, 246.
——, and Butler, S. (1946): *Ibid.*, **51**, 387.
Allison, G. G. (1943): *Sth. med. J.* (*Bgham, Ala*), **36**, 821.
Bushby, S. R. M., Catterall, R. D., and Williamson, Mary (1955): *Brit. med. J.*, **i**, 78.
Catterall, R. D., and Nicol, C. S. (1957): *Ibid.*, **ii**, 29.
Evers, H. H. (1957): *The Practitioner*, **178**, 311.
Feinberg, J. G., and Whittington, M. J. (1957): *J. clin. Path.*, **10**, 327.
Goldberg, A. A., Shapero, M., and Wilder, E. (1950): *J. Pharm.* (*Lond.*), **2**, 20, 89.
Gourlay, E. (1955): *Brit med. J.*, **i**, 912.
Greenblatt, R. B. (1945), *West. J. Surg.*, **53**, 135.
Haler, D. (1957): *Antibiotic Med.*, **2**, 358.
Hampstein, P. (1935): *Med. Welt*, **9**, 1845.
Kean, B. H. (1955): *Amer. J. Obstet. Gynec.*, **70**, 397.
Kearney, W. (1952): *Brit. med. J.*, **ii**, 223.
King, A. J., Mascall, W. N., and Price, I. N. O. (1936): *Lancet*, **ii**, 18.
Lanceley, F. (1957): Paper read at the Symposium on Typing of Trichomonads, Medical Society for the Study of Venereal Diseases, October 25, 1957.
Liston, W. G., and Lees, R. (1940): *Brit. J. vener. Dis.*, **16**, 34.
——, and Liston, W. A. (1939): *J. Obstet. Gynæc. Brit. Emp.*, **46**, 474.
Pattyson, R. A. (1937): *N.Y. St. J. Med.*, **37**, 41.
Platt, G. H., Seaman, J., and Hadgraft, J. W. (1951): *Brit. med. J.*, **ii**, 452.
Stewart, H. C., Hughes, W. H., Thomas, E. G., and Nixon, W. C. W. (1957): *Lancet*, **ii**, 1028.
Tiessen, H. J. (1957): *Derm. Wschr.*, **135**, 548.
Whittington, M. J. (1951): *J. Obst. Gynæc. Brit. Emp.*, **58**, 399, 614.
—— (1957): *Brit. J. vener. Dis.*, **33**, 80.

SOME NEW TREATMENTS FOR PSORIASIS

By E. LIPMAN COHEN, M.B.

Dermatologist, Oldchurch Hospital, Romford, and St. Margaret's Hospital, Epping

It has been estimated that there are between a half and one million sufferers from psoriasis in this country. Although the general health of these people is unaffected except in a small minority, the resulting discomfort and embarrassment is enormous. Ingram (1954) has described a technique of treatment which, if generally and conscientiously used, would probably give the best results. Nevertheless, the daily need for a tar bath, ultra-violet rays, and a stiff paste make it outside the range of practical treatment for the majority. Above all it is too time-consuming and it needs facilities and staff which are not generally available. For these reasons it is worth considering what help may be obtained from some of the newer forms of treatment even though the results may fall short of Ingram's ideal.

As with all chronic dermatoses, the best results will never be obtained by treating only the disease. The patient is always more important than his disease and it is essential to try to discover, and, if possible, to eliminate or reduce, those factors, often peculiar to the individual, which cause exacerbations and relapses.

CYANOCOBALAMIN

Every few months a new treatment for psoriasis appears in the medical journals. The results claimed for it are wonderful, sometimes a few supporting articles appear, and then no more is heard of it. When I read the report by Ruedermann (1954) claiming good results with vitamin B_{12} (cyanocobalamin) I took it for granted that this was just another flash in the pan. He gave 1000 micrograms intramuscularly daily for ten to twenty days to 34 patients. The psoriasis cleared completely in 11, nearly cleared in 10, and improved in six of them.

The week after reading this report an elderly patient came to see me in the out-patient department. I asked what was wrong with her but she said she was perfectly well. A little surprised, I asked what I could do for her. She replied that there was nothing that I could do for her, but that she very much wanted to tell me her recent experience so that others might be helped. She had had psoriasis as long as she could remember and she had become so used to it that it did not trouble her. The physician had prescribed injections for her anæmia and, to her great surprise, her psoriasis had disappeared. She wanted me to find out the nature of the injections so that others with psoriasis might be cured. It was easy to find from her notes that she had been treated with large doses of cyanocobalamin.

This patient's story, coming shortly after reading an article on the subject, seemed too striking a coincidence to be neglected. I started treating patients with severe or resistant psoriasis with daily (except Sunday) intramuscular injections of 1000 mcg. of cyanocobalamin, the course lasting three weeks. The results have been gratifying. Nearly half the patients found that their skin cleared completely, sometimes after one to three weeks' delay. A similar

proportion found the injections completely ineffectual. In only a few did the psoriasis improve considerably without clearing.

In the past three years there has been a number of reports of the efficacy of this treatment. Rimbaud *et al.* (1955), for instance, treated 17 patients for three weeks. The skin cleared completely in nine and there was marked improvement in three.

LIQUORICE DERIVATIVES

Glycyrrhetinic acid, derived from liquorice root, was introduced into dermatological practice by Adamson and Tillman (1955). There followed a long controversy about its efficacy. Eventually, Colin-Jones and Somers (1957) showed that there were two good reasons for the differences of opinion which had been so forcibly expressed. In the first place the acid is a mixture of a number of isomers only some of which are biologically active and some of the preparations used are, in fact, without any biological activity. Secondly it has been assumed that its actions and indications for use were identical with those of hydrocortisone whereas this is not true.

Sulzberger and his colleagues (1953) found hydrocortisone useless in the treatment of psoriasis, but Goldman (1957) found that an ointment containing glycyrrhetinic acid ('biosone GA' ointment) gave him greater relief than anything he had previously used. Colin-Jones and Somers (1957), who gave an account of its chemistry and pharmacology, treated 24 patients with itching psoriasis with this ointment and five with 'tar biosone GA' ointment and all were much improved. Evans (1958) treated 13 psoriatics with 'biosone GA' ointment: eight cleared or improved greatly and three others improved. He then treated 12 more patients with 'tar biosone GA' ointment with salicylic acid: seven improved greatly and three improved.

My trials with glycyrrhetinic acid have all been with 'biosone GA' preparations—mostly with 'tar biosone GA' ointment. I treated 21 psoriatics, 8 female and 13 male, whose ages ranged from 9 to 61. Itching was troublesome in 11 of them. With treatment the itching departed completely in a few days in eight and was much decreased in two more. On the whole the objective changes seen in the skin were less than the marked relief of itching. Patients were seen at intervals of two to three weeks and treatment was changed at their first return to hospital unless improvement was marked. Of the 21 patients, four cleared completely, three of them in less than a month. There was marked improvement in eight, slight improvement in five, and no change in four. Perhaps these results would have been better if I had persisted longer.

AMINOPTERIN

Aminopterin is an inhibitor of connective-tissue and epithelial-tissue proliferation. It is a dangerous drug. It prevents wound healing, causes atrophy and ulceration of mucous membranes, and leads to alopecia. Gubner (1951) gave 1.5 to 2 mg. of it daily by mouth to 13 patients with psoriasis. Treatment had to be interrupted after 14 to 28 mg. had been given, because of ulceration in the mouth or abdominal cramps. The skin cleared but relapsed later. Rees, Bennett and Bostick (1955) tried to avoid adverse effects by limiting the dose to 0.5 mg. daily for twelve to twenty days. There was marked improvement in 80 per cent. of the patients.

I have used aminopterin only once. The most resistant psoriasis I have ever known was the burden of a school teacher, aged 25, who had been under my care for some years. I took her into hospital, kept her strictly in bed, and gave her 0.5 mg. daily for twelve days. During the first few days there was marked improvement though the skin never became anything like clear. As soon as the treatment stopped the psoriasis became as bad as ever. During the treatment the white cell count dropped from 8000 to 5,800 per c.cm., but it soon returned to normal.

CASABIANCA'S TREATMENT AND DISTILLED WATER

Casabianca (1953) introduced a new treatment for psoriasis for which he claimed outstandingly good results. The new feature was the use of cystine which he gave in cachets each containing half a gramme, one cachet three times daily. In addition he gave Fowler's solution, an old treatment of high repute in psoriasis; most dermatologists refrain from using it because it causes the appearance of multiple skin cancers years later. His ointments were of a traditional nature and contained oil of cade. There have been a few subsequent reports of good results with this treatment but, generally, it has not found favour. I have not tried it.

Bolgert and Chiapponi (1955) report a man with generalized psoriasis whose skin was cleared by the daily intramuscular injection of 5 to 10 ml. of distilled water; the patient was told the substance injected was obtained specially for him from Algeria!

CONCLUSIONS

It is always worth while giving a three-week course of cyanocobalamin injections. The results are quite unpredictable but are sometimes astonishingly good.

'Tar biosone GA' ointment (with greasy or non-greasy base) is the best treatment for psoriasis when itching is troublesome. It is well worth trying in the absence of itching because, on the whole, its efficacy is higher than that of any other colourless preparation.

Aminopterin is a dangerous drug, which should never be used for psoriasis outside hospital, as blood counts on alternate days are essential, and it is doubtful if its use is justified even then.

References

Adamson, A. C., and Tillman, W. G. (1955): *Brit. med. J.*, **ii,** 1501.
Bolgert, M., and Chiapponi, L. (1955): *Bull Soc. franç. Derm. Syph.*, **62,** 50.
Casabianca, J. (1953): *Ibid.*, **60,** 172.
Colin-Jones, E., and Somers, G. F. (1957): *Med. Pr.*, **238,** 206.
Evans, Q. F. (1958): *Brit. J. clin. Pract.*, **12, 69.**
Goldman, V. (1957): *Brit. med. J.*, **i,** 46.
Gubner, R. (1951): *Arch. Derm. Syph.* (*Chicago*), **64,** 688.
Ingram, J. T. (1954): *Brit. med. J.*, **ii,** 823.
Rees, R. B., *et al.* (1955): *Arch. Derm. Syph.* (*Chicago*), **72,** 133.
Rimbaud, P., *et al.* (1955): *Bull. Soc. franç. Derm. Syph.*, **62,** 509.
Ruedermann, R. (1954): *Arch. Derm. Syph.* (*Chicago*), **69,** 738.
Sulzberger, M. B., *et al.* (1953): *J. Amer. med. Ass.*, **151,** 468.

GENERAL PRACTITIONERS' FORUM

A NOTE ON INFLUENZAL COMPLICATIONS IN AN EPIDEMIC

By W. P. GRIFFIN, M.D.
London, S.W.6

EVERY epidemic of influenza presents a challenge because of its wide and rapid spread, the varied symptomatology, the lack of specific treatment and the incidence of serious complications. The recent 'Asian 'flu' exemplified this well. Hospital, ambulance, home-nursing and laboratory services were severely strained by the spate of work and the 'flu casualties among their personnel. The difficulties were intensified by the incidence of complications among the cases. The impression gained in a London practice, and from the experiences of others, was that complications were encountered more often than in other recent epidemics—though admittedly it is difficult to obtain decisive data.

CLINICAL FEATURES

Approximately 90 per cent. of the cases were straightforward and responded well to bed rest, salicylates, plenty of fluids, and anti-coryzal inhalations where indicated. The remainder formed the complicated and the bad-risk groups, the latter being mainly patients with chronic bronchitis, bronchiectasis, debility or cardiac conditions. Fulminating cases occurred, and, indeed, one marked the start of the epidemic in this practice with dramatic suddenness.

A young West African collapsed in the waiting-room, bent double with epigastric pain. He was inarticulate and in obvious distress. His temperature was 102°F. (44.4°C.), pulse 140, and respirations 20 per minute. As a 'query acute abdomen' he was immediately removed by ambulance and admitted into hospital. By the next day the diagnosis was corrected—and the epidemic was truly with us.

The majority of those who reported to the surgery were simple cases; so, too, were many of those visited in their homes. An appreciable number, mostly in the latter group, had pulmonary complications. There were 18 in whom bronchitis was severe enough to require special treatment. Two frank lobar pneumonias in elderly patients who lived alone were sent into hospital. Three lobar pneumonias and three broncho-pneumonias were treated at home. Two true cases of encephalomyelitis occurred, exhibiting high fever, delirium and transient voluntary-muscle paralysis of one limb, with subsequent neurasthenic debility for about three weeks (these closely resembled some of the Royal Free Hospital epidemic cases of 1957). There were numerous instances of muco-purulent extension into the middle ear, especially in the young. In all, 660 cases of influenza were seen and 9 per

cent. of these were primarily bad risks or developed complications requiring special treatment.

TREATMENT

By predetermined policy it was decided to treat all patients at special hazard, by reason of pre-existing disease or complications, with penicillin, the safest of the antibiotics, in combination with sulphonamides—in the form of 'distaquaine V sulpha' (phenoxymethylpenicillin with sulphadimidine and sulphamerazine). Adults of average weight were given three 'distaquaine V sulpha' tablets six-hourly for four days with plenty of fluids. All the patients made rapid and complete recovery, including the three admitted to hospital. In fact there were no deaths throughout the whole series.

DISCUSSION

In adopting this line of therapy one was, of course, aware that it was not consistent with the teaching of those purists who would only have drugs prescribed singly, and who would withhold antibiotics or sulphonamides until the particular pathogen has been shown to be sensitive. But the pressure and urgency of such a situation as this brook neither delay nor oversophistication of method. One is faced with a large number of patients who are so ill that, if the disease process is not speedily arrested, their condition will become serious, if not grave. The pathogen may be difficult to obtain if not indeed inaccessible. Sensitivity tests take time, and in epidemics the resources of the excellent Public Health Laboratory Service and of the hospital bacteriologists are strained to the utmost. It appears, then, not only politic but imperative in general practice to take avoiding action.

To this end the first line of counter-attack is unquestionably oral phenoxymethylpenicillin, which in correct dosage has been shown in a host of reports to be as fully effective as the injected antibiotic. It has the advantage of sparing the patient the discomfort of injection—especially important in children—and of saving the over-pressed doctor a number of visits. Further, allergic reactions which may occur due to procaine or other adjuvants in depot penicillins are avoided. The second line is the sulphonamides, and even the academic pharmacologists recognize that a good case has been made for combining two or more of these owing to their different solubilities. As the mode of bacterial suppression of these drugs differs from that of penicillin it is surely reasonable to emulate the classical tactics of the battle of Cannæ and attack from two sides in a pincer movement. If the analogy is perhaps far fetched, at least the procedure answers the pragmatic criterion—it works.

It is undisputed that sensitivity tests are of great value and they should be made whenever possible, and certainly so when there appears to be any delay in response to therapy. But in this group of infections one should not wait for a report before starting treatment, the disease process should be arrested as soon as possible. One is not faced here with the difficulty so common in tropical medicine, that is, to begin antimalarial therapy in

fever before the parasite has been seen in the blood may make accurate diagnosis extremely difficult for a long time. It may also be mentioned that, although *in vitro* sensitivity tests are most informative, their correlation with *in vivo* action is possibly rarely complete. The *vis medicatrix Naturæ* must never be forgotten; drugs only reinforce the body's own defences.

SUMMARY

The main aspects of a clinical policy in the treatment of epidemic influenza in a single-handed London practice are outlined. One early apparently fulminating case was not diagnosed, but no other such particularly acute case occurred. Phenoxymethylpenicillin with sulphonamides was given to every patient who was considered to be a bad risk, or who developed secondary infections. This policy appeared justified in view of the stress of epidemic conditions, and the relatively small cost involved, and it is believed that it undoubtedly reduced the call on hospital and ancillary services and shortened the period of the patients' incapacity.

PREVENTIVE TREATMENT OF MIGRAINE WITH DIHYDROERGOTAMINE

By J. N. G. DRURY, M.B., B.Ch.
Blaby, Leicester

The migraine attack is one form of headache which has received extensive investigation over the years. The successful treatment of the acute attack is now well established, the most satisfactory method, from all points of view, being the oral administration of tablets containing ergotamine tartrate and caffeine ('cafergot'). It would, however, be much more desirable to find a means of preventing, or, failing this, reducing the frequency of, attacks, instead of merely aborting the attack when it occurs.

The basic etiology of migraine is still unknown; there may be one cause or, as is more likely, a number of causes. The actual mechanism of the headache, however, is accepted. It appears that numerous factors playing their parts in susceptible people trigger off the symptom-complex of the migraine attack. Numerous workers have studied the various factors involved: the migraine personality, the psychological aspect, its association with menstruation, epilepsy, and salt and water retention, to mention but a few. Any measures for prevention have been directed at correcting one or more of these known associations, but no definite method has emerged. Of these associations the psychological aspect has probably received the most attention, therapy being directed at removing emotional tension and persuading the patient to adopt a less perfectionistic attitude towards life. It does appear that in modern medicine an increasing number of patients are

visiting their doctors complaining of symptoms referable to emotional stress of some kind.

Numerous workers over the last few years, on the Continent and in the United States, have used dihydroergotamine as a means of preventing

Case No.	Age in years	No. of years a migraine subject	Attacks per year		Preventive dose in drops	Subjective comments
			Before DHE therapy	After DHE therapy		
1	26	4	36	36	25	Moderately improved
2	48	30	48	12	Not known	" "
3	32	22	24	12 to 24	20	" "
4	55	41	24	6	20	Greatly improved
5	34	9	24	3	3	" "
6	46	30	8 to 9	4	12 to 14	" "
7	32	12	12	Nil	9	" "
8	32	9	24 to 36	2	10	" "
9	44	32	12	4	15	" "
10	31	11	24	4	10	" "
11	34	2	52	12	15	" "
12	36	School days	36 to 48	Nil	DHE discontinued	" "
13	26	2	52	12	10	" "
14	43	25	36 to 48	12	25 to 30	" "
15	31	6	24	6	15	" "
16	38	3	36	2	20	" "

TABLE I.—Results of dihydroergotamine (DHE) therapy in 16 patients with migraine.

migraine attacks (Bartstra, 1946; Spühler, 1946; Chapuis, 1948; Kral, 1948; Dalsgaard-Nielsen, 1949). Their work indicated that dihydroergotamine was a useful prophylactic measure for the migraine sufferer. No reports have appeared in this country to my knowledge, apart from a letter I wrote to the *British Medical Journal* in 1954, in which I was able to say that in all my cases the interval between migraine attacks had been lengthened and the severity of the attacks diminished by using dihydroergotamine. This article is a continuation of the work mentioned in that preliminary report.

CLINICAL MATERIAL AND METHODS

Sixteen patients were studied in this trial: fourteen women and two men. They were patients in a general practice who attended for relief of their migraine attacks. No attempt was made to differentiate between menstrual migraine and the intermittent types, the sole object being to try to demonstrate a reduction in the number of attacks, without reference to the severity of the individual attacks or to the migraine type. All patients were encouraged not to change their mode of life in any way other than by taking the prescribed drug. The patients were given dihydroergotamine in the form of oral drops, the average dose being 10 to 25 drops before retiring. A questionnaire was then sent to the patients, which they were requested to complete, giving their own impression of the effect of the treatment on the frequency of their attacks. The material from the questionnaires is summarized in table I.

DISCUSSION

Of the total of 16 patients, no less than 15 showed a reduction in the frequency of migraine attacks. Of these 15 patients, two obtained complete abolition of their migraine, although one (case 12) could not be claimed as a success for dihydroergotamine as she became pregnant during the course of the trial and treatment was discontinued. Only one patient (case 1) failed to obtain a reduction in the frequency of her attacks. The large number of women in this series, fourteen as against two men (cases 3 and 6), is noteworthy, although in such a small series this could not be regarded as significant. The preventive dose varied from 10 to 25 drops. The subjective comments of the three patients in whom reduction in the frequency of attacks was not obtained, or was only slight, were mostly referable to the severity of the actual attacks. This, of course, is irrelevant so far as the object of this trial is concerned, but I felt it worth commenting on the subjective 'moderate improvement' when little or no reduction in the number of attacks took place. It is interesting to note that dihydroergotamine drops gave relief from the actual migraine attacks of those patients taking the drug as a prophylactic, if a therapeutic dose of 60 drops was taken at the start. No attempt is made to record this effect.

From these results dihydroergotamine emerges as a prophylactic drug of definite therapeutic effect. The rate of success is too high to be purely coincidental. A larger series would be a stronger confirmation of this drug's usefulness, but, unfortunately, from the point of view of this work, the number of migraine sufferers in any one general practice is not great. If this report, with its clear indication of the effect of dihydroergotamine in migraine prevention, stimulates further work on this subject it will have served its purpose and may well lead to the more effective treatment of migraine—prevention being always better than cure.

SUMMARY

Sixteen migraine sufferers treated with dihydroergotamine drops have been studied. Two patients obtained a cessation of attacks, thirteen a marked reduction, and only one failed to respond favourably to the treatment. One of the two patients who obtained complete relief became pregnant during the course of the trial and the administration of dihydroergotamine drops was discontinued. This patient is therefore not considered. The dihydroergotamine was administered as oral drops before retiring, the average dose being 10 to 25 drops.

References

Bartstra, H. K. G. (1946): *Ned. T. Geneesk.*, **90**, 1786.
Chapuis, J. P. (1948): *Schweiz. med. Wschr.*, **78**, 1125.
Dalsgaard-Nielsen, T. (1949): *Ugeskr. Læg.*, **111**, 1426.
Drury, J. N. G. (1954): *Brit. med. J.*, **i**, 286.
Kral, V. A. (1948): *Schweiz. Arch. Neurol. Psychiat.*, **62**, 128.
Spühler, O. (1946): *Schweiz. med. Wschr.*, **76**, 1259.

RABIES IN NORFOLK

By P. S. BARCLAY, *M.C.*, M.R.C.S., L.R.C.P., D.A.

Cromer, Norfolk

A CHANCE remark made to me by an elderly patient has revealed a link with an outbreak of rabies, and led me to study the incident itself and the later eradication of the disease from this country.

THE TRAIL OF THE MAD DOG

At about eleven o'clock on the morning of Saturday, June 14, 1890, a clumber spaniel, said to have belonged to a lady in Felixstowe, crossed over into the south-east of Norfolk by Homersfield bridge, near Harleston. Soon after, it bit two small boys, one of two years and the other of ten years. Wandering north, by seven o'clock that evening it was within four miles of Norwich when it bit two more children, a girl of twelve and a boy of nine, and later on reached Bracondale on the outskirts of the city, where another girl of ten and a young woman were similarly attacked and injured.

The dog then turned back again, for by six o'clock the next morning it was seen in a village six miles to the south where it snapped at a man with a wheelbarrow, and an hour or so later had wandered another three miles and bitten two persons and attacked a postman whose trousers had saved him from abrasions. In the course of the morning the dog bit another boy a little farther on and, after allowing itself to be caught and shut up in a shed, escaped and ran down the railway line to the village of Tivetshall, where it nipped in the arm a little boy of six who was out gathering wild strawberries on a fine Sunday morning. The next victim was to be the last. She was a girl of seventeen whose cries summoned her betrothed who, gun in hand, gave chase and, finding the animal lying exhausted in a ditch near New Buckenham, shot it shortly after mid-day.

Thus, in twenty-four hours the little beast had covered a distance of not less than 50 miles, having already crossed the county of Suffolk (fig. 1). During that time it had bitten at least ten persons.

AND SO TO PARIS

Following a declaration by the veterinary surgeon at Harleston, who performed a post-mortem examination, that the dog had been suffering from rabies, the injured were identified and eventually eight were sent to Paris for treatment at the Pasteur Institute. Among these was the little boy from Tivetshall who, sixty-eight years later, told me of his experiences.

The same afternoon he had gone to the doctor who had cauterized the wound in his forearm, and a day or two later a policeman came to his house in search of his mother to tell her that arrangements had been made for him

to go to Paris. One party had already left, so he had to be escorted. His guardian was a nurse from Norwich who was waiting for him at the station where he joined the London train, and twenty-four hours later delivered him safely at the boarding house in Paris where the others were already

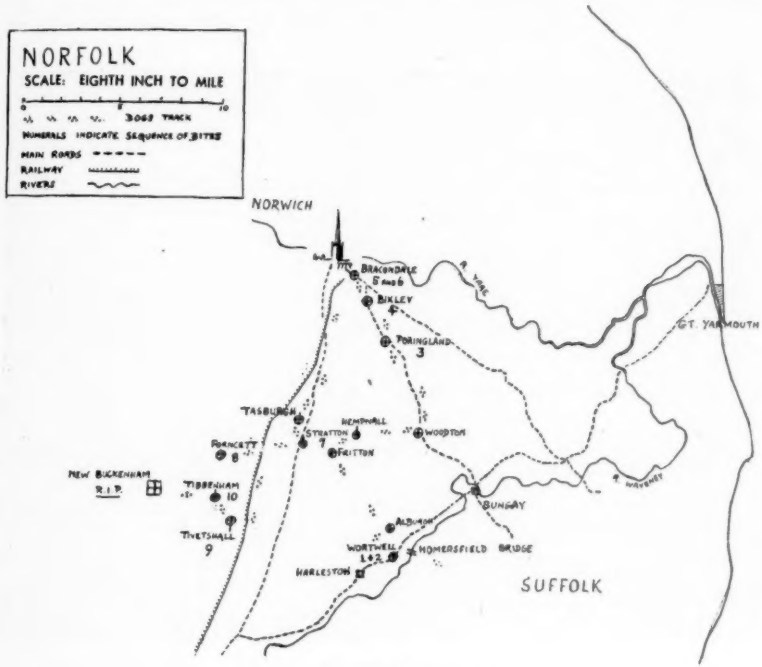


FIG. 1.—The trail of the mad dog.

established. Here the young girl of the party must have taken him into her special care for during the next ten days she wrote two letters to his mother. The first, dated 1889 in error, was written on June 23 (fig. 2).

'Just a few lines to tell that your little boy is getting better he is getting use to us all now he was strange the first day or to he sleeps well and eats well he is with me all day and I see that he is all right at night we have to go to the doctors every morning about eleven o'clock . . .'.

TREATED BY PASTEUR

At eleven o'clock each morning they attended the Institute (fig. 3) where they were led into a waiting-room to sit until their names were called. With the assistance of an interpreter full particulars were taken: their name, address, when bitten, by what kind of dog, whether it had been proved mad, whether through clothing; the name of the doctor who dressed the wounds, the nature of the treatment and whether they had ever been bitten by a dog

on a previous occasion. They would then be led through into another room where Pasteur himself, remembered simply as an old man (in fact he would have been 67 years old), wearing a little smoking cap (fig. 4), was sitting in a wooden armchair while behind and above him, presumably on some sort of gallery or dais, were young men and women watching.

The little boy was brought to stand before the great man, pinioned on

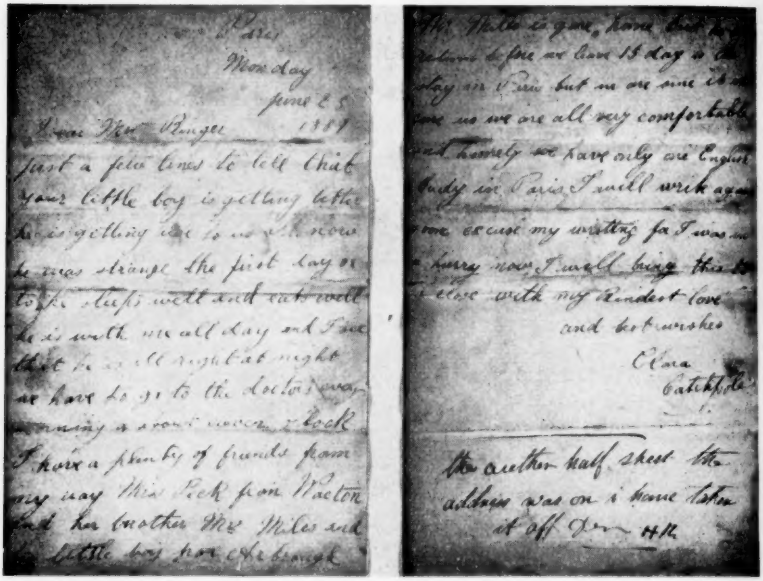


FIG. 2.—A letter from Paris.

each side by an attendant holding his arms outstretched while from behind a third held his head. Pasteur was then handed a syringe and, never speaking a word, performed the inoculation himself, injecting three times, twice on one side of the abdominal wall and once on the other. The recollection that someone held a cone-shaped roll of paper ready to thrust into any protesting mouth was almost certainly a misinterpretation of a gag held as a precaution against tongue biting. Deliberate and unnecessary physical restraint was obviously foreign to the principles of the clinic. Another patient in the same group from Norfolk remembers particularly how, when treatment was being given, Pasteur sometimes stood by to help to console frightened children.

The ordeal was then over for the day, the rest of which was spent in exploring an exciting new city, but it had to be endured for fourteen consecutive weekdays. Curiously enough, in this case, there is no recollection of any great pain, rather than the hurt of any injection is recalled the preliminary pinching of the skin.

His claim not to have cried out can be believed, but we know he was good from a second letter that was written to his mother on the 27th:—

'Just a few lines to tell you that your little boy is getting on well he was very fretful the first day or two he is very young to be so far from home he is such a good boy now and is enjoying himself very much he go out with us every day he has got over his worst of his pinch now and he stand it better than I could he will get like fat in another week . . .'. And a reassuring P.S.: 'The time won't be long'.

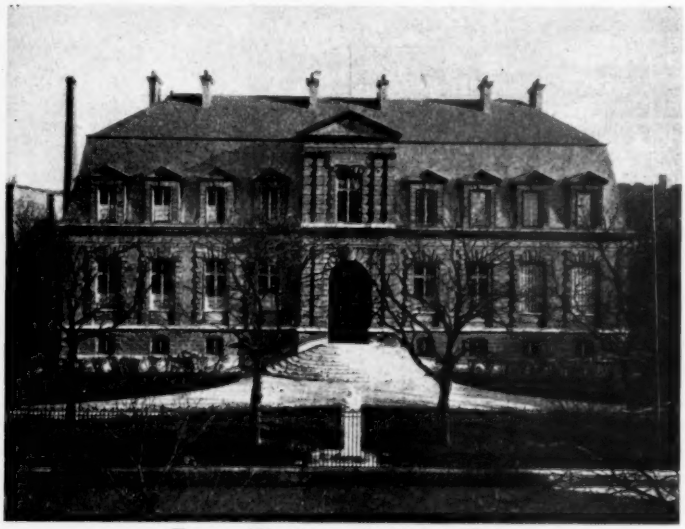


FIG. 3.—The Pasteur Institute in Paris.

When at last the time came for him to return he was alone again and had to be shepherded home. He was left at Victoria where a label, which he still possesses as a souvenir, tied to his jacket served to identify him to the police who were expecting him. Under the benevolent eye of the Law he was cleaned and fed before being taken to Liverpool Street to be put in charge of the guard on the Norwich train.

Thus could it be said that eight lives were preserved for there were no fatalities from that incident. Surely a credit to spontaneous human enterprise and sympathy so long before the birth of a Welfare State from within the sheltered protection of which one might take such an episode for granted.

A DREADED DISEASE

Rabies was endemic throughout the country and was recognized as a dreaded and dreadful disease. It was notorious for several reasons, not least because it was a threat that was increasing in incidence. During the thirty-eight years immediately preceding 1891, out of a total of 939 deaths from the disease the annual average had risen from 8 to 45. In the Metropolitan

district alone, during the years 1887-88-89 the police had killed 141, 190, and 330 dogs, of which 27, 49, and 123 had been shown to be rabid while the number of deaths registered in London for the same years had been 2, 3, and 7. It may well have been the grim details of one of these cases that were reported in the *Eastern Daily Press* of July 15, 1889:

'A man entered a tavern near the Elephant and Castle and shortly afterwards was taken ill. A Police Constable was called in and suspecting that the symptoms were those of Hydrophobia he called a Doctor. At about 5.30 the man began to breathe heavily when the sound resembled the growling and barking of an infuriated dog. He snapped at and tried to bite the persons surrounding him. He was then conveyed to St. Thomas's Hospital. It required several officials aided by police to strap him to the patient's chair. At the sight of one of the police the patient became so infuriated that although chained to the chair he shook and trembled all over and then caught by his teeth his right encased hand. His condition resembled an acute stage of madness accompanied by rigors and it required five men to hold him down for examination. Subsequently he was confined by straps and strait jacket and watched by attendants especially employed in cases requiring restraint.'

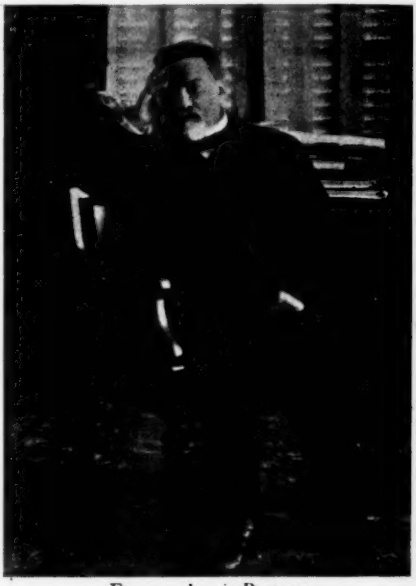


FIG. 4.—Louis Pasteur.

While the disease remained notorious on its own account it was gradually becoming more so as the result of the great tide of individual and collective human effort which on the one hand had already achieved the means of combating the infection itself and on the other was eventually to lead to its suppression and entire eradication from this Island. In 1885, Louis Pasteur had shown his great discovery when he treated by inoculation an Alsatian boy called Joseph Meister who had been bitten by a mad dog. With a few individual exceptions this had been accepted and acclaimed by the medical world of the time. Sir Victor Horsley, for instance, reading a paper entitled 'On Rabies' before the Epidemiological Society, concluded: 'It is clear that M. Pasteur has succeeded in diminishing the percentage risk in being bitten by a rabid dog from 15 to 1.36'.

THE PRINCE OF WALES ACTS

Nor was the medical profession alone in its acclamation. In June 1889, the Prince and Princess of Wales visited the Institute in Paris where they were received by Pasteur and his son. Here they witnessed inoculations and

were told of the work done. In the previous twelve months 1,673 persons bitten by dogs had been treated. Of this number, 1,483 were French, the rest from other countries. Thirteen of that number had later died, but it was said that these had begun treatment too late. The Prince was so struck by what he saw that he said he would endeavour to procure the opening of a similar Institute in England, believing it to be a blessing to mankind. At that time only in the United States and Russia had similar institutes been established. He shortly found the appropriate occasion to express his ideas at home.

At the beginning of the following month, under the auspices of the Society for the Prevention of Hydrophobia, a meeting was convened at the Mansion House, presided over by the Lord Mayor. The purpose was to hear statements from representatives of scientific and medical men in the country as to the efficiency of the treatment discovered by Pasteur, and how the Society might expedite it. To this meeting the Prince of Wales wrote a letter expressing his opinion and pointing out that 200 British subjects had been successfully and gratuitously treated during the past two and a half years. Resolutions were carried in favour of establishing a fund for the purpose of making a suitable donation to the Pasteur Institute and providing the expenses of British subjects requiring treatment in Paris but unable to pay for their own passage there. Subscriptions already announced included 100 guineas from the Prince and amounted to £1,030. It was resolved that the Government should be invited to introduce without delay a bill for the nation-wide muzzling of dogs. There was at the time a good deal of criticism directed at the inadequacy of the law as it stood. It was appreciated by the medical and veterinary profession that with stringent national regulations the disease could be wiped out, as had recently been achieved in Sweden.

The Muzzling of Dogs Act (1871) gave restricted powers to magistrates and police to control straying dogs and impose muzzling orders in their divisions, and under the powers vested in them by the Rabies Regulation of the Contagious Diseases (Animals) Act the newly formed local authorities could impose similar restrictions, but to no real national benefit with a disease with an indefinite, but certainly long, incubation period of 25 to 40 days. The time was yet to come when a government department itself was to take advantage of this same Act.

In 1890, Norfolk had had no rabies for fifty years. Now public reaction was immediate and from Harleston telegrams were sent to M.P's requesting them to use their influence in having the muzzling order put into effect in that district at once. The Harleston Bench had acted spontaneously and exercised their powers within that division almost immediately. Six days after the incident the local papers reported that the clerk to the local authority, which must have been the County Council, had received a telegram from the Privy Council asking if his Authority had made any regulations under the Rabies Order. The matter was referred to the contagious disease subcommittee who immediately issued the appropriate

order. They had been urged by the special adviser of the Board of Agriculture to impose the Order throughout the County, but eventually applied it to the southern half only. Within twenty-four hours of the drafting of the order, 2000 handbills and 500 placards were in course of being distributed. Elsewhere, the combined committees of the East and West Suffolk Councils made the Order compulsory throughout the whole of that county. At the end of the month the Norwich Town Council followed suit.

NORFOLK PAYS THE BILL

Public authority seldom acts as quickly as individual enthusiasm. This latter force, readily assisted by the police, had speedily marshalled and dispatched eight persons to Paris within not much more than a week, the first three reaching their destination within three days. Nor was this all. Very shortly a letter appeared in the local press announcing the opening of a fund to be called the 'Pasteur Patients' Fund' for the financial relief of those sent:—

> 'So far as can be ascertained at present, the total expenses of the eight patients will amount to about £100. An application has been sent to the Mansion House Fund, but from a letter received this morning it seems uncertain as to how far the fund will be in a position to give considerable help. The relations and friends of the patients several of whom belong to the labouring class are all anxious to do what they can to assist, but I feel sure that the Public . . .'.

The statement was true indeed. My patient's father was a maltster earning about £1 a week. A budget of the child's expenses had been prepared (fig. 5) and found to total the formidable sum of £14 8*s.* 10*d.*! It will be noted that there is no charge for the course of injections.

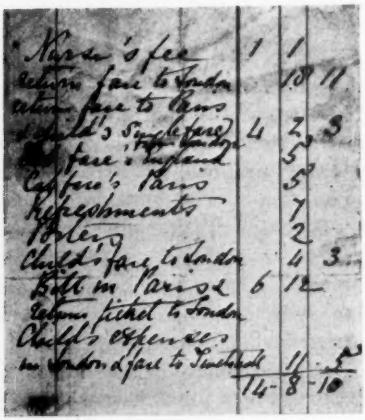


FIG. 5.—The bill.

	£	s.	d.
Nurse's fee	1	1	0
Return fare to London		18	11
Return fare to Paris and child's single fare from London	4	2	3
Cab fare—England		5	0
Cab fare—Paris		5	0
Refreshments		7	0
Porters		2	0
Child's fare to London		4	3
Bill in Paris and return ticket to London	6	12	0
Child's expenses in London and fare to Tivetshall		11	5
	£14	8	10

The appeal was successful. A total of £117 10*s.* 4*d.*, including £20 from the Mansion House Fund, was raised. This covered all expenses with a small balance for a donation to the Pasteur Institute.

So the episode closed and now, in conclusion, it is salutary to consider how the disease was eradicated from this country long ago.

EPILOGUE

In April 1897, the Board of Agriculture determined to make an effort to exterminate rabies. A year before they had appointed a departmental committee for the purpose of inquiring into, and reporting upon, the working of the laws relating to dogs. The findings had been issued, and recommended that the Board should take such action forthwith by exercising directly the powers they possessed under the Diseases of Animals Act. The anticipated extirpation of the disease should be followed by a general Collar and Registration of Dogs Order, to procure their more efficient control, whilst statutory power should be invested in some authority with a view to regulating and controlling importation.

Against much public opposition the muzzling order was enforced in a determined manner over a wide area and maintained until six months had lapsed after the occurrence of the last reported case. By May 1900 it was deemed possible to relax the order completely and the disease was declared extinct although during the same summer it reappeared in Wales and several counties were once more restricted. The year 1901 became the third in succession in which no death from rabies was registered in the United Kingdom. After this successful outcome a lapse occurred the following year when two more cases were reported, but they were the final flicker of a dying threat. They were to prove the last recorded in this country, for ever since we have remained entirely free from the disease.

During the same period an Importation of Dogs Order had been made whereby a licence was required to permit their being brought into the country, and this imposed the condition that all dogs should require a period of six months' quarantine detention. The licensing laws in relation to dogs also became established as we know them today.

A relaxation of these regulations could well allow the reintroduction of rabies into this country. It remains endemic in many parts of the world, and cases have occurred of dogs developing the infection while in quarantine. We are protected from the ravages of a horrible disease by simple measures whose strength depends upon the stringency of their observation. Human emotion may be capricious and blind to reason. When chance momentarily draws aside the curtain of time, allowing us a glimpse into the past, we do well to heed the lessons that our forefathers learned by bitter experience.

THE GENERAL MEDICAL COUNCIL 1858–1958

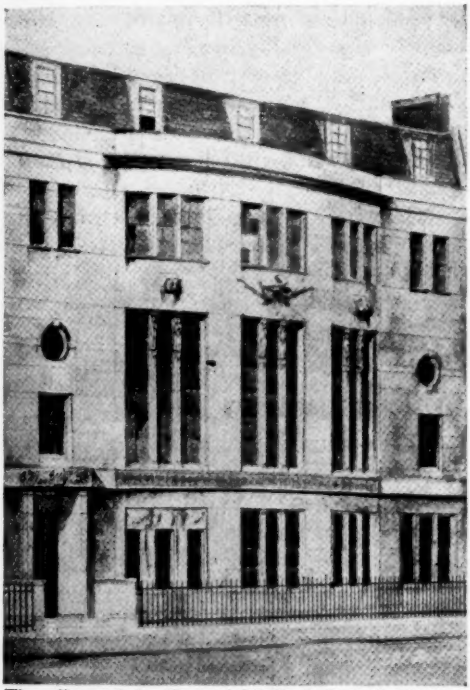
By J. G. McCRIE, O.B.E., T.D., M.B., F.R.C.P.Ed.
Dean of the Faculty of Medicine, University of Sheffield

THE present is an opportune time to survey the work of the General Medical Council during the first century of its existence, for the Council was set up by the Medical Act of 1858 and held its first meeting on the 23rd of November in that year. Changing times, and the evolving ideas of the Council itself as to its own nature and purpose, have led to numerous other legal enactments in this sphere, the chief landmarks being the further Medical Acts of 1886, of 1950, and of 1956. The last-named, being a consolidating measure, could not fundamentally alter the law. Nevertheless, since it specifically repeals practically all previous legislation in the field of medical education, registration and discipline, and systematizes and codifies all that it is desired to retain of the contents of these enactments, it constitutes a measure of the greatest importance; indeed, it is under the Medical Act (1956) that the General Medical Council has operated since January 1, 1957. Lest, however, the words systematization and codification should suggest undue rigidity, it should be mentioned that certain modifications and improvements, of whose desirability the Council had become conscious, have already been secured by means of the Medical Act, 1956 (Amendment) Act, 1958. And there is no reason to suppose that what would seem, on the whole, to have been a path of enlightened progress will not continue.

EDUCATIONAL ACTIVITIES

The primary purpose of the original Act of 1858 was, of course, to provide a ready means whereby the public could distinguish between a practitioner in respect of whose training, competence and good professional standing there was some sort of statutory guarantee and one in respect of whom no such guarantee existed. During the last century we have become so accustomed to the idea of a 'registered medical practitioner', and to all that flows from this concept, that it is difficult to visualize the conditions of medical practice before it came into being. Such difficulty has recently been well met by the publications of Newman (1957) and of McConaghey (1958). It is clear from these that during the first half of the nineteenth century the idea of the general practitioner as we know it today was already evolving independently, but progress was greatly accelerated when the 1858 Act set up a 'General Council of Medical Education and Registration', empowered to maintain a 'Register' to which admission could be secured only by persons possessing qualifications which the Council (after various procedures of inquiry which it was statutorily empowered to make) was prepared to regard as satisfactory. Equally, the Council could direct 'the erasure from the Register of the names of persons criminally convicted, or judged by the

Council, after due inquiry, to have been guilty of infamous conduct in any professional respect'. Thus, the foundations of the situation as we know it today were laid. It is probably not altogether surprising, in view of the reasons which had brought the Council into being, that in its earlier period it appears to have been much more concerned with its educational functions than with disciplinary matters. Such preoccupation is reflected in its original name, and, although many years later the Act of 1950 recognized what had for long been customary, and shortened the title to that of 'General Medical Council', the change is not without its regrettable side.



The offices of the General Medical Council, Hallam Street, London, W.1. The building, which was designed by Mr. Eustace Frere, A.R.I.B.A., is scheduled as a building of special architectural or historic interest in the Borough of St. Marylebone.

Naturally, order could not be created out of chaos immediately, and a defect of the 1858 Act was that it permitted the entry to the Register not only of persons qualified both in medicine and in surgery, but also that of those qualified *either* in medicine *or* in surgery. The chief advance brought about by the Act of 1886 was that it limited entry to the Register to persons who had passed an examination—(and one which could now be 'inspected' in a more formal fashion than that allowed by the 'visitation' prescribed by the earlier Act)—in the *three* subjects of medicine, surgery and midwifery. This, from the examinational aspect, is still the position, and the next important step, from the point of view of the relation of the G.M.C. to undergraduate medical education, was the granting, by the Act of 1950, of authority to visit medical schools. The older Acts had empowered the Council to 'require information' from Licensing Bodies about their courses of instruction, but not to carry out personal visitation of schools. (It may be remarked in passing, as an example of the need for, or at least the desirability and convenience of, the (consolidating) Act of 1956, that, before the

passing of this measure, the pre-clinical examinations were visited under the Act of 1858, final examinations inspected under that of 1886, and medical schools visited in virtue of that of 1950.)

FREEDOM TO MANŒUVRE

The considerable preoccupation of the Council in its early days with matters of educational policy has been noted, and at one time it seemed—particularly before the Act of 1886 had done something to ease the task of the Council in fulfilling the duties placed upon it by the original Act—as if, in relation to curricula and examinations, the tendency might be in the direction of uniformity and rigidity. This phase is now long past, and it has been repeatedly emphasized by Presidents from the Chair that the Council has no wish to impose any rigid educational pattern upon any medical school. It is, of course, true that the Council has the responsibility of ensuring that any individual to whom a registrable qualification has been granted by a Licensing Body has received such an education, and passed such examinations, as guarantee his proficiency in the practice of medicine, surgery, and midwifery, and that to this end it has been granted considerable powers in relation to the visitation and inspection of medical schools and examinations. It is also true both that the Council periodically issues 'Recommendations as to the Medical Curriculum' and that, in the past, these Recommendations have been so precise and detailed that Licensing Bodies may well be forgiven for having treated them in practice (as well as referring to them in speech) as 'Regulations'. Even this phase is now passing, and recent Presidential utterances, as well as the wording of the latest (1957) Recommendations themselves, make it abundantly clear that, within certain broad and reasonable limits, teaching and examining bodies are not only free, but are encouraged, to make experiments in medical educational methods. This is a considerable, and happy, move away from the attitude which it seemed originally that the Council might take up. The latter may well have been a necessity of the times, but these times were probably the least happy or productive in the Council's existence.

To those unversed in medical legislation, the question may well occur of how, if the Council exercises (apparently) so light a control over teaching and examining bodies, it in fact adequately discharges the responsibility entrusted to it by Parliament in relation to medical education. The answer is that, if it did appear to the Council (as a result of the processes of inquiry, visitation and inspection already referred to) that the qualification granted by some particular Licensing Body was *not* such as to guarantee in a holder of that qualification 'the requisite knowledge and skill for the efficient practice of his profession', the Council could report the facts to the Privy Council, which might then direct that the qualification in question should no longer confer the right of admission to the *Medical Register*. The potentiality of such a drastic sanction still exists, but the relations between the Council on the one hand, and the teaching and examining bodies on the

other, are now (and no reason can be seen for thinking that they will not continue to be) such that any matters for discussion between the two are likely to be put forward, and to be met, with reasonableness and understanding, and ultimately to be settled in a manner satisfactory to both sides.

THE 'PROVISIONAL' MEDICAL REGISTER

Before the passing of the Medical Act of 1950, the educational responsibilities of the General Medical Council had been limited to the period ending with the granting of a registrable medical qualification and the admission of an individual to the *Medical Register*. As is well known, the Act of 1950 provided for an individual's admission in these circumstances only to a 'Provisional' Register. This entitles him to practise as a house-physician or house-surgeon in certain recognized posts in certain approved hospitals, and he becomes fully registered only after such a period of service has been certified as satisfactory by the Licensing Body which originally granted the registrable qualification. It is perhaps not so generally understood that, although the Council (subject to approval by Parliament and by the Privy Council) prescribes the minimum period of provisional house-post service (at present twelve months) which must elapse before full registration can be secured, the approval of institutions, and the recognition of posts and certification of satisfactory service therein, is a matter entirely for Licensing Bodies. There is no such thing as 'G.M.C. recognition', and the 'List' published by the Council is merely, and does not purport to be other than, a convenient index.

Having now dwelt at some length on educational matters, we may conclude by referring briefly to some other aspects of the Council's responsibilities.

RECIPROCITY

It was one of the provisions of the original Act of 1858 that admission to the *Medical Register*, then created, conferred the right to practice in any part of Her Majesty's dominions, and considerable thought has been given continually since that time to the question of the registration of persons possessed of medical qualifications granted elsewhere than in the United Kingdom, and to 'reciprocity' between the United Kingdom on the one hand and, on the other, both 'foreign' countries and territories within the Commonwealth. Especially since the introduction of the compulsory intern year (in some parts of the world before it was adopted in this country), the difficulties have not all been one-sided. Much of the Council's time, or more particularly that of some of its committees, is devoted to this matter, whilst ambassadorial journeys undertaken by the President, or by visitors nominated by the Council, have been very fruitful. In this connexion it may not be generally known that *temporary* registration, for the purpose of taking up a particular appointment, may be secured with little difficulty by properly qualified teachers or postgraduate students from abroad, who are thus spared the inconvenience (and perhaps the legal disability) of being

'unregistered persons'. This has been so since the passing of the Medical Practitioners and Pharmacists Act of 1947 (now incorporated as necessary in the Medical Act, 1956), though the main part of this measure related in fact to a different question.

DISCIPLINARY AND OTHER ACTIVITIES

If, in its earlier period, the Council tended to concentrate more upon educational than upon disciplinary matters, there followed a stage when the reverse at least appeared to be the case. The educational side tended to become more of a committee matter, although the Council as a whole (until the Act of 1950) dealt with penal business. The emotional appeal of the latter, too, was naturally that which caught the public imagination, and it is doubtless with the drama of erasure from the *Register* that the General Medical Council is chiefly associated by the public at large. It is probable that the 1950 Act, by establishing the Medical Disciplinary Committee to deal with penal business, and thus freeing the Council as a whole for other matters, may have re-directed its mind towards the educational side, although it was of course this very Act which, *de jure* as well as *de facto*, removed the word 'education' from the Council's name.

It may be convenient here to refer to certain other provisions of the 1950 Act which have not yet been mentioned. The membership of the Council was considerably enlarged. In 1858, it had been 24; since 1950 (though admittedly the increase had come about in stages) it has been 47. The number of Crown nominees (six in 1858) became eight, three of whom had to be non-medical. Non-medical Crown nominees, however, were not entirely an innovation, since one had been appointed as early as 1926. Representation of Universities and Licensing Bodies remained related to the number of such bodies; but the number of 'direct representatives' of the profession (i.e. medical members elected by the postal votes of doctors resident in England and Wales, Scotland, and Ireland) was raised from five (first prescribed by the Act of 1886) to eleven. Further, important provisions were introduced regarding the number of 'direct representatives', as well as of lay members, who must sit upon the disciplinary committee. 'A medical practitioner', someone said at the time, 'has the right to be tried by his peers, rather than by his professors'. The legislative opportunity was also taken to empower the disciplinary committee to take evidence upon oath, and to compel by subpœna the attendance of witnesses or the production of documents. It was enacted that any finding of fact in matrimonial proceedings in the British Isles should 'be conclusive evidence of the fact found' in relation to any inquiries by the disciplinary committee. Finally, the important right of appeal (to the Judicial Committee of the Privy Council) was granted against penal erasure from the *Medical Register* by the disciplinary committee.

DENTISTRY

No account of the Council's work in relation to education, registration, or

discipline would be complete without notice being taken of its responsibilities in connexion with dentistry during the years 1878 to 1956. During this whole period the Council was responsible for standards of dental education, carrying out visitation of dental examinations, and issuing Recommendations as to the dental curriculum. After the Dentists Act of 1921, much of the routine disciplinary work was transferred to the Dental Board then created, although the final decision as to erasure from the *Dental Register* still rested with the Council. Now, with the Dentists Act of 1956, the dental profession has reached full constitutional independence, possessing its own General Council, though its origin as a branch of surgery is still recognized by the right of the General Medical Council to nominate six of its number to sit as members of the General Dental Council when matters of education and examination are being discussed.

THE BRITISH PHARMACOPŒIA

Finally, brief reference may be made to the responsibility of the General Medical Council for the publication of successive editions of the *British Pharmacopœia*. Since 1929, this duty has been discharged through a 'Commission' of persons possessed of expert knowledge of the fields in question, and the chairman of the Pharmacopœia Commission has been the director of operations. The responsibility of the General Medical Council, however, is indicated by the method of selection of members of the Commission, and by the fact that formal effect is given to the latter's decisions through the Council, as advised by its Pharmacopœia Committee. New editions of the *Pharmacopœia* come out at present at approximately five-yearly intervals. Traditionalists may regret that, in the 8th (1953) edition, Latin disappeared from the main titles of monographs, whilst, from 1963 onwards, the apothecaries will be displaced by the metric system.

CONCLUSION

Space does not permit of more being said. This is unfortunate because, even among members of the medical profession, there seems to be considerable misapprehension about what, in various circumstances, the Council does (or does not) do, should (or should not) do, or indeed, because of its constitution and nature, is permitted (or not permitted) to do. A point may therefore be emphasized which was made by the President in a public address in Sheffield a few years ago. The membership of the Council is now fairly broadly based among practising doctors, academic teachers, and the lay public, and it is to be hoped not only that these will keep the Council informed about the views of those they represent, but equally that they will discharge similar functions in the opposite direction, 'explaining and commending the Council's decisions to their colleagues at home'.

References

McConaghey, R. M. S. (1958): *J. Coll. Gen. Practit.*, **i**, 267.
Newman, C. (1957): 'The Evolution of Medical Education in the Nineteenth Century', London.

CURRENT THERAPEUTICS

CXXXI.—WOUND DRESSINGS

By WILLIAM GISSANE, F.R.C.S., JOHN BULL, M.D., and DOUGLAS JACKSON, M.D., F.R.C.S.

Birmingham Accident Hospital

'I dressed their wounds, God healed them'.—Ambroise Paré (1510-90).

Wound dressing was probably the earliest form of surgical treatment. The linen cloths and bandages recommended in Egyptian papyri achieved their objectives of soaking up and stopping bleeding, covering the wound from sight and to an extent protecting it from further damage.

In 1537, Ambroise Paré, serving with the army of Francis I when it was besieging Turin, ran out of oil of elder (then used scalding hot to cauterize open wounds), and replaced it with a 'digestive' made of yolk of eggs, oil of roses and turpentine. Next day he examined the two groups of dressings. Those patients who had been cauterized were in great pain, feverish and the local lesion (not surprisingly) was grossly swollen. The other group had rested well, were in little pain and the wounds were without inflammation and swelling. Empirically he had found the value of a mild and possibly an antiseptic wound cover. Yet it was not until 1867 that Lister, influenced by Pasteur's work, revolutionized surgery by the introduction of the antiseptic treatment of wounds. First-intention healing then became the rule rather then the occasional exception, and deaths from erysipelas and hospital gangrene were much reduced. Professor Volkmann, addressing the First International Medical Congress in 1881 said that for forty years before Lister nearly all patients with compound fractures died of them and that even those with small open wounds often succumbed to them. The search then began—and still goes on—for an antiseptic capable of destroying contaminating bacteria on or in the wound, without injuring the vital qualities of the exposed tissues.

Reddish (1954) summed up the position today as follows: 'No such ideal antiseptic has yet been found. The best that can be done is to disinfect the surrounding skin, cleanse the wound surgically, ensure a good circulation, dress the wound infrequently, put the part at rest, use specific chemotherapy and rely upon the natural defences and healing processes of the body'.

WOUND HEALING

The healing of a typical wound through the whole thickness of the skin involves four processes:—

(1) Dead tissue (if the wound is not treated surgically) is removed by autolysis phagocytosis and gross separation.

(2) In the depths of the wound, vascular endothelium migrates into the cavity, forming capillary buds which carry with them fibroblasts and macrophages. The resultant granulation tissue fills the wound cavity.
(3) Contraction of the wound reduces the raw area.
(4) Migration of epithelial cells over the granulation tissue completes the cover provided the area is not too large and that it is kept clean. If the dermis is undamaged, this migration occurs early and may provide a thin cover within a few hours. In deeper wounds, epithelial repair must await the filling of the wound cavity by granulation tissue. Excessive heaped granulation tissue can also delay epithelial migration.

The granulation tissue is subsequently reorganized into fibrous tissue and the full thickness of the epidermis is generated by proliferation of the initial single layer. At the same time further contraction of the wound occurs. This is probably better known as cicatrization, to distinguish it from the early and more rapid process of contraction (Arey, 1936; van den Brenk, 1956). Wound dressings must give adequate protection to these delicate processes of cellular migration and growth, and prevent added infection until the wound achieves sound epithelial cover.

THE SOURCES OF WOUND INFECTION

The intact skin of the body, particularly its exposed surfaces, is continuously contaminated by a wide variety of pathogenic organisms. In the polite manner of coughing and sneezing hand-skin contaminants may be nasopharyngeal streptococci and staphylococci. After another physiological act they may be the coliform group of organisms. Many skin contaminants are the result of various occupations: for example, in farm workers the anaerobes of tetanus and gas gangrene, in hospital staff the widest variety of pathogenic and non-pathogenic bacteria. Healthy intact skin continuously cleanses itself by drying and by the bactericidal action of its unsaturated fatty acids. Yet it is probable that the source of the majority of primary wound contaminants is either from the surface of the patient's own skin or his covering clothes; comparatively few result from bacteria on the wounding instrument.

The wounding instrument or the method of wounding may so damage the tissues as to favour the subsequent development of infection. Dead tissue provides an excellent culture medium, and tissue that has suffered a significant impairment of its blood supply is less able to withstand infection. The object of early wound surgery is the *gentle* removal of all dead and badly damaged tissues together with all inert foreign material, leaving the wound in such a healthy state that its natural defences can be brought to bear against any contaminants. The ideal time for wound surgery is within an hour of wounding: i.e. before contamination has developed into infection. Antibiotics can lengthen this interval. The major danger of infection of all wounds, particularly large wounds, is from added infection from a wide variety of sources. The sources are the nose, throat, hands and clothes of the patient or his attendants, unclean instruments and, in long dressings of

large wounds, from the air itself. In special dressing stations where the air can be filtered and sterilized and a gentle non-touch technique followed by well-trained teams, the hazards of infection from all sources can be largely eliminated. Yet added infection remains the great danger to all wounds, particularly in ambulant and ward patients. It can be minimized but not completely eliminated by sound methods of wound cover.

Such are the degrees and varieties of wounds and the interval between wounding and plenary dressing that no single method can meet the requirements of every type. Further, it is now generally accepted that no wound dressing can do more than provide the tissues with the most suitable condition for physiological healing.

FUNCTIONS OF DRESSINGS

It is convenient to consider the functions of the various components of a dressing in terms of their relation to the raw area. Next to the wound it is important that the material should not be incorporated into the tissues as a foreign body, and it should not become adherent as the wound dries. The aim is to provide a smooth, non-irritant, non-toxic surface which will permit exudate to pass through it. The layer outside this should absorb this fluid; its volume, in a burn for instance, may be large, and high absorbency is demanded of this layer. Gamgee, in 1880, proposed his sandwich of absorbent wool and gauze for this purpose, and similar layers of absorbent cotton-wool or cellulose are used in dressings for burns. If the dressing becomes completely soaked with fluid, it ceases to be a barrier to infection (Colebrook and Hood, 1948), and the dressing will then require changing. The outer layer of a composite dressing must retain the whole structure in position and apply whatever pressure is required for the wound. Commonly this pressure is achieved by the use of an elastic bandage applied under slight tension. Although experiments have shown that the pressure so applied is not well sustained, since the deeper layers of the dressing tend to accommodate themselves to the tension and so relieve the pressure upon the wound, the tendency for the elastic bandage to follow the retraction of the dressing is helpful in maintaining large dressings in position. The whole dressing should provide adequate splintage to the wound. Clearly if the delicate migrating epithelial cells are subjected to excessive tearing strains, they will suffer damage and healing will be delayed. The bulk of the dressing is usually sufficient to splint the wound, but there may be special indications for further immobilization. In children it is often advisable to apply a light plaster cast outside a large dressing to prevent disturbance of the dressing by the patient. The outer layers should preferably resist soiling, wetting and mechanical damage.

The whole dressing should cause minimum inconvenience consistent with maintaining the conditions for healing. If work is to be continued, then it is important that the dressing should resist the likely hazards, whether

they be wetting by fluids and oils, catching fire or being caught in moving machinery.

MINOR WOUNDS

Minor skin wounds are a major national problem, both in industry and in the home. Squire (1951) has estimated that half a million such injuries, requiring at least one first-aid dressing, occur each day in this country.

In the decade, 1940-49, infection of minor wounds probably resulted in more lost time from work than any other form of industrial injury with the exception of fractures. In Birmingham, during that decade, 19 deaths occurred from infection of such industrial injuries (13 from septicæmia and six from tetanus) accounting for 5.8 per cent. of all deaths from industrial injury in that City.

Scales and his colleagues (1956) suggested the following requirements for the dressing of minor wounds.

(1) It should have a high porosity to water vapour (to keep the wound dry).
(2) It should not adhere to blood clot or to the granulating surfaces, nor should it allow the permeation of capillary loops. It must, however, absorb free blood and/or exudate and give protection to the wound.
(3) It should be a barrier to the passage of micro-organisms.
(4) It should be capable of holding the contours around a joint during movement.
(5) It should be unaffected by domestic and industrial fluids.
(6) It should not produce a tissue reaction when applied to normal skin or a granulating area.
(7) It should be capable of being sealed to the skin.
(8) It should be capable of being sterilized.
(9) It should be available at low cost.

Traditional dressings fail on one or more of these counts although, as will be mentioned later, recent developments of plastic materials promise to meet those requirements almost completely.

FIRST-AID DRESSING OF MAJOR WOUNDS

The hazards of added infection to all open wounds are now well recognized. Although pathogenic organisms may be introduced at the time of wounding, as often as not they are added to the exposed areas after wounding and from a wide variety of sources. The very early cover of all wounds is therefore an essential part of first-aid treatment. Colebrook's dictum that 'the longer a wound remains open (and uncovered) the more certain it is to be infected' should be displayed in all first-aid stations.

First-aid wound cover must be readily at hand and easily and quickly applied. In a very extensive burn the immediate cover of the whole body with a freshly laundered sheet is sufficient protection during transport to hospital. For a large, but less extensive, wound any freshly laundered linen material of sufficient size, for example a pillow case, affords an efficient temporary protection. In some types of wounds, particularly of the extremities, bleeding may be an additional problem in first-aid treatment. It is usually more safely controlled by a pressure dressing than by a tourniquet.

There is still an important first-aid need for the manufacture of easily applied long stockings and long gloves of one of the non-adhesive new materials (e.g. P.V.C., nylon or terylene-type film of a micro-porous structure) for the quick wound cover of compound fractures of the extremities. There is also a place for a moulded splint of soft foam rubber or one of its synthetic counterparts, to provide comfortable splintage for the fracture and so prevent further tissue damage during transport to hospital.

DRESSINGS OF CLEAN CLOSED SURGICAL WOUNDS

The adequate dressing of sutured, clean, surgical wounds in all parts of the body by the traditional methods of gauze, cotton-wool and bandages of various types continues to present problems of maintaining complete wound cover during the healing process. All too commonly the bandage loosens and the cover dressing wanders off the wound. To a degree this can be prevented by tying the dressing over the wound or by holding it firmly in position by some form of adhesive strapping. Such dressings are both bulky and uncomfortable. These traditional dressings for clean, closed, surgical wounds, are now replaced by many surgeons, who have tried the method extensively, by covering the wound with a thin film of an acrylic resin dissolved in a mixture of acetic esters and applied preferably as a spray: e.g. 'nobecutane'. This results in a thin, elastic, transparent and adhesive dressing which remains in position until the skin sutures need removal; it is then peeled off with forceps and the sutures removed in the usual way. This film is flexible, strong and waterproof. Patients can move about freely and take a bath safely before the sutures are removed. If it cracks, re-spraying by a nurse is simple; to prevent cracking the film should not be too thick. If infection occurs under the film it is quickly recognized and the film is then peeled off and the more traditional type of dressing used.

Rob and Eastcott (1954) report only one wound infection of a mild degree in 200 wounds dressed by this method. Our own experience of its use is equally satisfactory. Before the film is applied absolute hæmostasis is essential, for oozing from the wound strips off the plastic film, and wound apposition must be exact. Added operative time necessary to secure both is always worth while whatever type of dressing is used. Finally, the skin surface must be quite dry for the plastic will not adhere to a wet surface.

DRESSING OF WOUNDS CLOSED BY FREE SKIN GRAFTS

Skin grafts are the ideal wound dressing to cover areas of full-thickness skin loss, and so quickly re-establish the waterproof and protective cover of normal skin. When a graft of the requisite size is cut to cover the whole raw area, certain requirements for the dressing, if used, still remain. Immediately over the graft an open-mesh textile treated with oil, such as 'tulle gras', permits exudate to pass freely through and prevents adhesions of the

dressing to the graft. Outside this a layer of moist cotton-wool carefully moulded into position keeps the graft firmly but gently against its bed. This second layer is pressed firmly into position by a gauze roll, dry wool and an elastic bandage to keep the whole dressing in place and to provide splintage.

If a skin graft is submitted to strain it may be dislodged partially or completely from its bed: an important cause of graft failure. It should be noted, however, that pressure is not an essential requisite to the 'take' of any skin graft. If hæmostasis is complete, and the recipient area not concave, so that 'tenting' of the graft is likely to occur, if the patient is cooperative and the area not submitted to pressure or movement likely to dislodge the graft, then skin grafts can 'take' without the support of any dressing. Dressings therefore are usually protective. Grafted areas, particularly those of the lower extremity, should be protected from gravitational strains and treated by bed rest until they consolidate.

DRESSING OF OPEN WOUNDS

Large wounds must sometimes be left open for days or weeks, and there are several reasons for this. The wound may be a partial-thickness skin loss burn, the patient may have insufficient donor areas to provide efficient grafts to complete skin cover, or, rarely, the patient may be too ill for the anæsthetic and operation. In these cases alternative methods of local management are called for.

For the majority of such wounds, recent and old, a dressing which is an efficient bacterial barrier is desirable to prevent initial or further colonization with pathogenic organisms. This may incorporate an antibiotic, preferably one which does not produce allergic reactions and to which sensitive organisms do not become resistant. The choice of antibiotic in a particular case will vary according to the findings of bacterial examination of the wound flora and the most serious expected contaminants; for instance, group A β-hæmolytic streptococci are the most troublesome organisms in hindering the take of skin grafts. The dressing may also incorporate a mechanical barrier, such as a thick layer of dry cotton-wool, or a sheet of plastic which is impermeable to bacteria while being permeable to water vapour. Whatever the components of a dressing for such serious wounds, it should be effective in preventing contamination and mechanical trauma and it should be comfortable and remain efficient for several days.

Some wounds, because of their position and perhaps the restlessness of the patient, are difficult to dress effectively. This applies especially to burns of the face, buttocks and perineum. In such cases use should be made of other means which lessen the multiplication of organisms on the wound surface. Mechanical cleansing is perhaps the most obvious of these. This may simply take the form of daily dressings with thorough cleansing at each application; or the whole patient may be bathed in saline or 'lux', and

debris and scabs removed. Use may also be made of the antibacterial effect of dryness, light and a cool temperature limiting the growth of some organisms such as *Ps.pyocyanea*. This is the basis of the exposure treatment of burns, but a similar effect can sometimes be provided by a dry closed dressing in contrast to one with a cream.

There is a difference in the eschar which forms on an acute burn and on a granulating wound. In the former the scab is composed of dead dermis, in the latter of fibrin and leucocytes. But in both cases the scab may be beneficial or harmful. If pus collects beneath it, it should be removed repeatedly and without delay; if, on the other hand, there is no sign of suppuration beneath it, it is often a good cover for the healing wound which can be left exposed or simply covered by a protective dressing.

A third type of cover is the homograft. For the extensive burn, when more than 10 to 15 per cent. of the body surface remains uncovered after as much as possible has been auto-grafted, homografts have the distinctive benefit that they prevent infection, exudation, and painful dressings in the area covered. Such grafts can be obtained from any donor who is free from transmissible disease, such as syphilis, malaria, or jaundice, or even from the recently dead; and they remain for an average of two-and-a-half weeks before beginning to break up and come off.

The choice of the method of local dressing in large wounds such as burns which must be left open is a matter for individual decision. 'What', one should ask oneself, 'is the best local treatment for this wound, in this patient, in this environment?' Factors which must be considered are the site of the wound, whether the patient should be treated in hospital or not, the climate, the available privacy, the availability of dressings and dressing-room staff, the availability of adequate ward supervision for efficient splinting, the bacterial flora of the wound and the facilities for isolation, the age of the patient and his need for ambulation, the need to examine the patient repeatedly and the prevention of hyperpyrexia. These are but some of the factors which will influence the doctor's choice, and there is no reason why different sites of the body should not be treated differently at the same time. All these methods of management are only ways of temporizing with the least possible damage, until the wounds can be closed permanently with autografts.

TRADITIONAL DRESSING MATERIALS

Since the time of Lister, dressing materials have been centred upon absorbent cotton gauze. This was introduced in 1871 as 'an elegant and convenient form of modified oakum' and was incorporated in Lister's dressing as a vehicle for a mixture of carbolic acid, paraffin and resin. The absorbency of gauze can be tested by the method recommended in the *British Pharmaceutical Codex*, which depends upon its rate of sinking in water, or more satisfactorily by the quantity of fluid which the material can

absorb; this has been termed 'absorbing capacity'. As normally available, gauze is made from staple fibre, the threads of which are liable to fray and become incorporated in the drying wound fluids. An alternative to gauze for immediate application to the wound is a textile treated with oily materials such as 'tulle gras'. This has the useful property of permitting exudates to pass freely through the open mesh while the oily material tends to prevent adhesion of the healing tissues. Absorbency is offered by cotton-wool, and this forms the intermediate layer of the traditional wound dressing. Its particulate structure makes it unsuitable for immediate application to the wound, and its absorbency varies from sample to sample and depends upon the detailed fibre structure. Alternatives to cotton-wool are various cheaper forms of cellulose such as wadding.

The outer layers of traditional dressings have usually been the convenient and cheap cotton bandage. This has ample tensile strength for most purposes but no elasticity, and being flat does not easily adapt itself to curved surfaces. Developments have included the elastic bandage which incorporates either a wool fibre (crêpe bandage) or a rubber strand. Such bandages are much superior to those entirely of cotton for retaining large dressings and for applying sustained pressure.

NEW DRESSING MATERIALS

New dressing materials have become available chiefly as a result of the great development of the plastic industry. This has provided a new range of textiles as well as various films with potentially useful properties. Among the textiles it is now possible to have continuous filament rayons, terylenes and nylons which obviate the troubles due to staple fibres becoming detached, as in cotton gauze. Some of these fibres are also water repellent, and therefore less likely to become adherent to wounds. Investigation of the best type of weave of such materials has been made by Owens (1946). He showed that a rayon fabric dressing with a fibre of 30 denier and warp and weft of 114 x 114 caused little disturbance of underlying granulation tissue and a reduction of pain and bleeding. It is suggested that the capillary buds of granulation tissue are too large to penetrate the mesh of such a dressing and that therefore adherence is diminished. Some adhesion, however, does occur, and such dressings may need to be moistened before removal.

Plastic substances in solution can be applied to wounds so as to form a transparent protective film. Collodion (a solution of nitrocellulose) has been used for many years; more recently acrylic resins and vinyl chlorides have been developed for this purpose. Unfortunately, suitable solvents are rather irritant although this is not of great importance for small or sutured wounds. The preparations now marketed in aerosol form further diminish exposure to the solvent. Among the plastic films cellophane was investigated by Bloom (1945) and shown to have promising properties in the treatment of burns. The film is permeable to water vapour and forms a complete barrier

to the entry of bacteria. Cellophane, however, has the disadvantage of relative rigidity and brittleness. A film which combined the same satisfactory permeability properties, but which had advantages in elasticity and strength was the nylon type 8 film investigated by Bull and his colleagues (1948). Dressings of this material were tested by Schilling and his colleagues (1950) for use on small industrial wounds, and found to compare favourably with other types. A more recent development has been the use of a P.V.C. film manufactured so as to have a micro-porous structure. This film improves again on the nylon film in respect of elasticity and handle; it takes adhesives well and is now the basis of a successful commercial dressing ('aerostrip') which appears to incorporate most of the desirable features for the treatment of minor incised wounds (Scales *et al.*, 1956). For larger wounds a film of terylene in which minute holes have been punched has been recommended for immediate application to the raw area. In commercial composite dressings this film is backed by an absorbent cellulose layer and dressings of this type have advantages in avoiding adhesion to the wound while permitting adequate absorption of exudates. Other developments have included substitution of the oily material of 'tulle gras' with water-soluble glycol derivatives which can be a vehicle for antibiotic or chemotherapueutic agents. These dressings are satisfactorily non-adherent initially, but since the water-soluble material tends to be washed away, the dressing is liable to become adherent to the wound as it subsequently dries.

For the outer covering of dressings a notable advance has been the introduction of various types of adhesive plasters, some of which are completely waterproof and others are permeable to varying degrees. These are now available with many different mechanical properties of rigidity and elasticity in one or more planes. There are disadvantages in the application of waterproof plastic which is completely adherent to the skin. Skin troubles under such adhesives are not uncommon and, though often attributed to sensitivity, are probably more often due to the simple mechanical sealing of the skin combined with irritation due to pulling of hairs and other skin structures. On the other hand, true sensitivity to various materials in adhesive mixes does occur. Recent development of a fenestrated application of the adhesive should reduce the effects of mechanical irritation and sealing. An important use of adhesive plasters is to lock the layers of a dressing and so maintain it in place. This has now obviated many of the more complex bandaging procedures described in the older text books.

CONCLUSIONS

Dressings are the most frequent form of surgical treatment in hospitals and are numbered in millions a year. Outside hospitals the dressing of minor wounds is numerically an enormous surgical problem. Intelligent appreciation of the needs of different types of wounds and the comparative virtues of various dressing materials should make a valuable contribution to

surgical practice. No single dressing is to be expected for all wounds: wet or dry, clean or infected, sutured or left open. The variety of suitable dressings is increasing and will continue to do so as new materials are investigated.

Perhaps one should remember that not a few surgeons today are returning to a 'no dressing' routine, relying on the accurate and careful suture of the wound, absolute hæmostasis and the soft dry eschar that result from wound exposure. This trend is a criticism of the existing standards of hospital dressings.

Adequate wound dressings involve other problems than a choice of the appropriate materials. Considerable economies in the time taken in dressing a wound and improvements in dressing technique can be achieved by providing each surgical ward and the outpatient department of hospitals with well-planned, self-contained dressing stations, as described by Gissane and his colleagues (1944). It is probable that the heavy load of pathogenic organisms present in most hospitals is in part, at least, the result of dressing wounds in the busy atmosphere of a general surgical ward, and the very haphazard methods of disposal of dirty dressings. Both these obvious hazards could be eliminated by the building of modern self-contained dressing stations wherein dirty dressings can be immediately destroyed on their removal from all wounds. Safe, small and comparatively inexpensive electric incinerators are now in use in many women's locker rooms at sports clubs and in factories and should be capable of adaptation for the disposal of dirty dressings in hospitals. The ease with which wound dressings can be destroyed may well have a bearing on the dressing materials of the future.

References

Arey, L. B. (1936): *Physiol. Rev.*, **16**, 327.
Bloom, H. (1945): *Lancet*, **ii**, 559.
Bull, J. P., Squire, J. R., and Topley, E. (1948): *Ibid.*, **ii**, 213.
Colebrook, L., and Hood, A. M. (1948): *Ibid.*, **ii**, 682.
Gissane, W., Williams, R. E. O., and Miles, A. A. (1944): *Brit. J. industr. Med.*, **1**, 90.
Owens, N. (1946): *Surgery*, **19**, 482.
Reddish, G. F. (1954): 'Antiseptics, Disinfectants, Fungicides and Sterilization', Philadelphia.
Rob, C. G., and Eastcott, H. H. G. (1954): *Brit. med. J.*, **ii**, 17.
Scales, J. T., Towers, A. G., and Goodman, N. (1956): *Ibid.*, **ii**, 962.
Schilling, R. S. F., Roberts, M., and Goodman, N. (1950): *Lancet*, **i**, 293.
Squire, J. R. (1951): 'Plastics Progress', London, p.267.
van den Brenk, H. A. S. (1956): *Brit. J. Surg.*, **43**, 525.

MINOR SURGICAL PROCEDURES

XII.—CIRCUMCISION

By REX LAWRIE, M.S., F.R.C.S.

Surgeon and Assistant Director, Department of Surgery, Guy's Hospital; Surgeon, Evelina Hospital for Sick Children

CIRCUMCISION is the operation of removal of the foreskin. It has been performed by various peoples for many thousands of years using various methods, some of which are still current. A circular scar is always left and it should not be possible for this to ride forwards over the glans, as contraction of the scar then leads to an appearance resembling the uncircumcised state and a recurrent phimosis.

INDICATIONS

Whilst there are a few genuine surgical indications for circumcision, in the vast majority of cases the indications have been connected with ritual, religion or fashion. In Great Britain the operation is unfashionable at present, especially among pædiatricians.

Surgical indications in the adult include paraphimosis, carcinoma of the penis and genital warts. Actual narrowing of the preputial orifice to such an extent that it obstructs the flow of urine and leads to gross ballooning of the prepuce, is an uncommon but splendid indication.

In the infant, obstruction to the passage of urine is occasionally seen, but more often the mother complains that he 'cries when he wants to pass his water', which is very different and probably of little significance. In the child, paraphimosis is again an important indication. Recurrent balanitis is another complaint for which circumcision is often performed, with doubtful wisdom. The complaint of a discharge of purulent material from the prepuce must be distinguished from a discharge of smegma which has been pent up by an adherent prepuce. Tense beads of this material can sometimes be seen and felt through the prepuce and may alarm the mother.

Phimosis is a common complaint often confused with two other conditions. The term should probably be reserved for true annular scarring around the preputial orifice. This may be the result of excoriation and ulceration of the prepuce or of repeated attempts at forcible retraction, as is not uncommonly advised by doctors, nurses and welfare centres. In some instances this leads to multiple radial fissuring of the preputial orifice, which heals with some infection and results in an organic stenosis. The two conditions which must be distinguished from this are:—(a) A narrow preputial orifice—the usual finding in babies referred with the label of phimosis. In these the penis and preputial orifice are both small and the prepuce cannot be easily retracted. There is no reason why it should be, and it is a more

effective protection for the delicate glans if it cannot be retracted. Evidence is accumulating that this is an almost normal state of affairs in infancy, which corrects itself as the child grows up and is not an indication for circumcision in the infant. (b) An adherent prepuce. In many infants the prepuce is not separated from the glans, and it is generally accepted that the plane of separation develops normally with the passage of time as the child grows up. Certainly no plane can be found, and the effect of forcible retraction of such an adherent prepuce is to strip the epithelium of some or the whole of the glans. Re-epithelization takes about a fortnight, as can be seen if stripping the prepuce is combined with circumcision, for the glans is then miserably sore and raw for about that time.

DISADVANTAGES

Whilst it is often easier to perform the operation than exorcize the emotional or religious grounds on which the parents base their request, it is important to be aware of the disadvantages and risks it entails. First it must be realized that there is a primary operative mortality which has been assessed at 17 per annum in Great Britain. Probably most of these are from anæsthetic accidents; others doubtless from sepsis; and there may be occasional deaths from conditions such as the unrecognized infant hæmophiliac who develops uncontrollable postoperative bleeding. Apart from this the main local drawback of circumcision is the hazard of a meatal ulcer from excoriation of the delicate glans against nappies. This leads to recurrent acute retention from crusting of the meatus and, when at length the lesion heals, may leave a very resistant meatal stricture. Unnecessary operations must always be avoided both on psychological grounds and because of the subsequent misery and behaviour disturbance. These are common after circumcision, particularly if the glans is sore or urination difficult for a long time afterwards.

CONTRAINDICATIONS

Besides the needlessness and disadvantages of circumcision there are some contraindications, the most important of which is hypospadias, as in this condition the tissue of the prepuce may be valuable for reconstructing the urethra, and should therefore be preserved. The other contraindication is concerned with choosing the right time. In infancy the response to trauma and sepsis is often not stabilized, with the result that an operation may lead to prolonged sepsis. For this reason elective operations should not be performed anywhere on an infant's body when there is a rash or pyoderma. A rash in the napkin area can often be cleared within a week or two by improving the local hygiene and laundering arrangements, and by adding a few crystals of permanganate of potash to the daily bath. Napkin rash is particularly troublesome from the age of six months until the child is dry; and in the winter months, when more clothing has to be worn, often in a stuffy atmosphere. This is a time when circumcision should be avoided if (as is usual) possible.

OPERATIVE TECHNIQUE

Whilst local analgesia in the form of a ring block of the base of the penis is entirely effective, general anæsthesia is almost universally preferred in both children and adults. The operation consists of five distinct steps:—

(a) *Retraction of the foreskin.*—This can usually be performed by a manœuvre which combines pulling the skin back with expressing the glans. Retraction must proceed backwards into the coronal sulcus all round, and smegma and other material are gently wiped away with gauze. A tight phimosis may occasionally need to be dilated by inserting the tips of a pair of mosquito forceps in the correct plane (but not into the lumen of the urethra). Separation of an adherent foreskin is facilitated, as the skin is drawn back, by the use of a blunt probe. Rough wiping with gauze is harmful to the delicate epithelium of the glans.

(b) *The skin incision* is then symmetrically marked out with ink or a scalpel blade. It should slant downwards and forwards parallel to the line of the coronal sulcus. There is no need for radical excision of skin, which, in some instances, may result in disastrous denudation of the shaft of the penis. The skin is then cut off along the line of the mark and discarded. It is most important not to damage the glans.

(c) *The mucosal excision* is then performed. A dorsal cut is made with scissors as far back as the coronal sulcus and is then carried round on each side with scissors, preserving a 2-mm. frill of mucosa.

(d) *Hæmostasis* is then obtained with mosquito forceps. The most constant bleeders are the dorsal vein and the frænal artery. These vessels are tied off with very fine catgut. Other vessels near the skin or shaft of the penis are likewise secured but those in the mucosa are usually insignificant.

(e) *The wound is then sutured.*—Four quadrantic fine catgut sutures are usually sufficient to obtain accurate muco-cutaneous coaptation, but as many others are added as necessary. It is an advantage to hold the first two sutures long while inserting the subsequent ones. No dressing is applied. The wound heals best if kept dry, and the traditional compound tincture of benzoin on ribbon gauze is best omitted as it may act as a tourniquet, and is sometimes difficult and painful to remove.

This technique is applicable to all cases—both children and adults, although in the latter more sutures are usually necessary.

COMPLICATIONS

Reactionary hæmorrhage is usually not severe but occasionally necessitates opening the wound, evacuating clot and tying the bleeding vessel. This can with advantage be performed under local infiltration analgesia.

Hæmatoma is a common but usually slight complication.

Sepsis is seldom serious, but can easily be promoted by the use of moist dressings or dirty wet nappies.

Rawness of the glans, lasting a fortnight, is the rule where it has been necessary to separate an adherent foreskin. Spontaneous healing is assisted

by keeping the area dry and well powdered, leaving off the nappies if possible.

Meatal ulceration with crusting and acute retention of urine is occasionally seen. It is necessary to bathe the crust off the urethra and institute a regime of keeping it moist and protected from friction until the ulcer has healed. This may be done by fixing in place a finger cot with the end cut off.

ALTERNATIVE METHODS

Jewish ritual circumcision, which has a long reputation of success, differs in some respects from the technique just described. It is performed when the infant is a week old, without anæsthesia. The foreskin is drawn down and held by the groove of a special guard, which is too narrow for the glans to run any risk of being included. The redundant skin is cut off with a knife and the mucosa split along the dorsum by the rabbi's thumbnail. The split is carried right into the coronal sulcus and the mucosa folded back over the cut edge of the skin. The excess of mucosa dries up and separates, so that once again the annular scar lies always behind the glans and recurrent phimosis cannot occur.

Other races, notably some African tribes whose culture is that of the Stone Age, perform circumcision by means of a sharp stone. The technique is crude, and sepsis and scarring sometimes necessitate a subsequent operation.

The dorsal slit operation is sometimes used to obviate the rather complicated surgical technique of a satisfactory circumcision and the hazard of hæmorrhage and sepsis. After separating the prepuce from the glans the former is divided along the dorsum as far as the coronal sulcus, hæmostasis is obtained and the cut edges sutured if necessary. The operation is also useful in cases of paraphimosis with gross œdema and a fear of spreading infection if a full circumcision were to be performed.

REVISION CORNER

BEDSORES

It is justifiable to preface any discussion on bedsores by stressing the very obvious fact that prevention is not only better than cure—it is a great deal easier. This is only a comparative statement, however, for the problems of prevention of bedsores are many, and may often be insoluble.

CONTRIBUTING FACTORS

As Guttmann (1956) points out, there are several factors, both intrinsic and extrinsic, which can contribute towards the development of bedsores.

Intrinsic factors are present in the very ill, aged, or otherwise enfeebled

patient; they comprise essentially the tendency to remain immobile in bed, and a lowered tissue resistance to pressure. Immobility results from a combination of causes—diminished capacity to appreciate sensations of pressure (and therefore the need for a change of posture), mental apathy and muscular weakness. These conditions obviously pertain to a much greater extent in paraplegic states, in which complete motor and sensory paralysis may be present. Diminished resistance of the tissues to pressure is merely one aspect of lowered body-resistance as a whole, and is the natural concomitant of old age or of serious illness. In paraplegic states lowered tissue-resistance to pressure is very evident, and is believed to be caused by loss of vasomotor control, resulting in paralytic dilatation and consequent capillary damage. This, combined with sensory and motor paralysis, affords a ready explanation of the frequency of bedsores in paraplegics, and we have little need to postulate the loss of 'trophic' nerve supply as a causative factor.

Extrinsic factors are local pressure, and maceration of the skin from prolonged contact with sweat, urine or fæces. The deleterious effect of such moist discharges on the skin cannot be doubted, but it seems probable that the part they play in the formation of bedsores is a relatively minor one. It is rare to see ulceration of any depth in the skin of the perineum, scrotum or thighs, even in the most neglected patient, and such superficial irritation as may be present in these situations clears up rapidly with ordinary nursing care. Much the more important factor would appear to be that of pressure —or rather of *compression* of the tissues which lie between the bed and the nearest bony surface or prominence. The traditional view which associated bedsores with bad nursing care *of the skin*, presumed that the initial lesion was in the skin. This may well be incorrect in a considerable proportion of cases. When a cutaneous slough has been excised or cast off, it is quite common to find in the underlying muscle a slough which is much larger, and apparently of longer duration, than the skin lesion. The work of Groth (1942) and Husain (1953) has shown that in experimental animals the skin and subcutaneous tissue are far less susceptible to pressure than the underlying muscle. The initial lesion may therefore be in the muscle. Vascular obliteration occurs during the period that pressure is being exerted, and is later followed by reactive hyperæmia, with increased capillary permeability; this in turn leads to extravasation and tissue necrosis. This possibility is not mentioned in order to decry the importance of skin care, but rather to emphasize the much greater importance of avoiding pressure.

PREVENTION

For the prevention and treatment of bedsores, two principles may be laid down. The first is to prevent continued pressure, especially against any uneven surface; the second is to maintain or increase the resistance of the skin, or to stimulate its healing power. The first of these ideals is the more important, and fortunately, by comparison, it is the easier to attain.

Avoidance of pressure.—I shall not weary the reader with a dissertation on the virtues of soft (but not sagging) mattresses, unwrinkled sheets, air-rings and air-beds, nor will I suggest that the patient's position should be changed every two hours, day and night. Such advice, which is to be found in every nursing manual, is surely a counsel of perfection, and represents an ideal which, except in specialized centres, is impossible to attain. There is, however, much we can do to minimize the effects of pressure. The two commonest sites for pressure are over the middle of the sacrum and over the sacro-coccygeal junction. The former takes the pressure when the patient lies flat in the supine position, and the latter when the patient is propped up in the semi-recumbent position. Pressure sores over the ischial tuberosities, acquired from pressure in the sitting position, are rare except in paraplegics. Guttmann has pointed out that a sliding or 'shearing' strain on the soft tissues overlying a bony prominence may be more damaging than direct pressure. This type of strain is particularly evident in the sacro-coccygeal region of a patient who is propped up in bed, but who exhibits the usual tendency to slide downwards. If it remains in position, a sponge-rubber or inflatable air-ring may minimize direct pressure, but it does little to reduce the shearing strain. The obvious remedy—and the only one—is to prevent the patient from sliding down the bed; this can be done by raising the foot of the bed on blocks, by placing within the bed a box or other object to act as a foot-rest, or by the old-fashioned 'donkey', fashioned by a bolster placed transversely below the thighs, and tied at each end towards the head of the bed. This last method has suffered an eclipse at the present time, because of the supposed risk that it may cause deep venous thrombosis, but such risk would appear to be greatly exaggerated.

The use of 'cotton-wool rings' to protect the heels from pressure, has little to commend it. These rings seldom stay long in position; even if they do, they may substitute a shearing strain for direct pressure, since, as the heel sinks into the ring, the skin becomes progressively more stretched over the bone. The most effective method of preventing pressure on the heels is to raise the calves on a soft pillow. This involves acceptance of the risks (if any) of causing thrombosis in the calf veins.

It is unfortunately easier for the attendants to nurse aged or chronically sick patients continually in bed, than to get them up for short periods each day. It is easier still when the patients themselves show no wish to leave their beds, and resent any suggestions to that effect. But the effort to get the patient up—even for a short time—should nevertheless be made, and the necessity for it explained to all concerned. The patient who is able to get into a chair for the bed to be made, should usually be able to stay in it for at least an hour or two. This should, if possible, be insisted upon, and any opposition be worn down. For such reasons, a suitable chair is as essential as a suitable bed. If the patient has to be continually in bed, he should (if his cardiac and respiratory condition allow) be allowed to lie flat during

the night. During the day, when he is propped up, sliding strain on the sacro-coccygeal region should be avoided by the measures described. Whether he is lying supine or semi-recumbent, the site of pressure can be varied by turning him, slightly or almost completely, to one or other side.

PREVENTIVE CARE OF THE SKIN

The benefits of soap, water, spirit and dusting powder in the prevention of bedsores have long been accepted, and such treatment has been employed as routine in most hospitals. Doubts as to its efficiency, however, have recently been cast by Bateman (1956) who noted that patients who were free from pressure sores after even long periods of bed-nursing in their own homes, soon developed such sores after admission to a geriatric hospital. In his preliminary report he records that the incidence of bedsores was immediately and significantly reduced by discontinuation of the classical routine treatment. He recommends the application of 'silicone vasogen' (20 per cent. polydimethylsiloxane in a water-soluble base). Washing of the skin, which does not remove the silicone preparation, is reduced to the minimum necessary for cleanliness. Further reports on this method of treatment are awaited with interest.

Urinary incontinence can be dealt with by an indwelling catheter, or (in the male) by the wearing of an appliance such as the 'simplex'. Fæcal incontinence is more difficult to control, but is less damaging to the skin.

TREATMENT OF THE ESTABLISHED BEDSORE

The first essential, of course, is to remove pressure from the part—too often, once again, a counsel of perfection, but as already indicated much can be done in this direction. The host of local applications which are advised indicates, only too clearly, that none enjoys any clear advantages, and the choice must depend upon personal preference. In my own experience, the threatened bedsore with no more than redness and œdema (which are reversible changes), or the early bedsore, with blistering or superficial ulceration, can be treated very satisfactorily by the application of 'elastoplast', provided that this is not allowed to become wrinkled by sliding pressure. When the skin has to be protected from moist discharges, waterproof strapping ('sleek') has proved effective. When infection is present, some form of moist compress (eusol or hypertonic saline) should be employed. For pyocyaneus infection, 2 per cent. acetic acid or phenoxyethanol is recommended. Any sloughs, whether consisting of skin, fascia or muscle, should be cut away until reasonably healthy tissue is exposed, for a sore covered with a slough is a classical example of a closed septic wound, from which toxic material is absorbed into the circulation. The various methods of plastic repair of bedsores, by the swinging of flaps from neighbouring parts, are outside the scope of this discussion.

For treatment of the 'healthy' or potentially healing bedsore, we return

inevitably to the avoidance of pressure—especially sliding pressure. Once this can be achieved, the choice of local application is probably of little importance. One bedsore may be stimulated to heal by moist compresses, another by medicated ointments or creams, whilst yet another may respond best when kept as dry as possible by the application of spirit and dusting powder. Any single treatment, after evoking an initially good response, may appear to lose its effect, and it is necessary therefore to ring the changes according to the results obtained.

References

Bateman, F. J. A. (1956): *Brit. med. J.*, **i**, 554.
Groth, K. E. (1942): *Acta med. scand.*, **87**, suppl. 76.
Guttmann, L. (1956): *Brit. J. plast. Surg.*, **8**, 196.
Husain, T. (1953): *J. Path. Bact.*, 66, 347.

ERIC L. FARQUHARSON, M.D., F.R.C.S.
Surgeon, Royal Infirmary, Edinburgh.

MALLET FINGER

MALLET finger is due to sudden forced flexion of the terminal joint of a finger while the extensor tendon is tense. As a result, either the tendon ruptures close to its insertion, or the posterior margin of the distal phalanx into which the tendon is inserted is avulsed. Power of extension of the distal joint is lost, and the distal phalanx droops down into 45° to 60° of flexion. Flexion power is normal.

ETIOLOGY

In men, a common cause is to stub the finger when catching a cricket ball, the middle finger being naturally that most commonly involved. In women, tucking the bedclothes under the mattress while bedmaking takes pride of place. The middle, ring, and little fingers are the common victims, the index much more rarely. Sometimes the trauma is quite trivial, suggesting uncoordinated spasm of the extensor muscle at the critical moment or previous degeneration of the tendon; occasionally there is no definite injury at all. It should also be remembered that when the distal joint is flexed the skin of the dorsum of the finger is stretched tightly over the very thin extensor tendon, and that there is almost no protective subcutaneous tissue; in these circumstances an apparently trivial cut from a sharp kitchen knife when washing up can quite easily sever the tendon over the joint.

The degree of pain in mallet finger varies surprisingly. Some may be almost painless within a few minutes; others, untreated, stay markedly painful for days or weeks. Those with an avulsed bony fragment are usually in the painful group.

TREATMENT

Diagnosis presents no difficulty. Treatment, in spite of what the textbooks say, is not always so easy. The principle is simple: to splint the finger so that the torn ends of the tendon come together and unite without lengthening. To procure this ideal the distal joint must be extended and the proximal interphalangeal joint flexed. A simple experiment on oneself reveals that if the proximal joint of a finger is passively held fully flexed all power of extending the distal joint is lost. In this position the central slip of the extensor tendon, by which the proximal joint is extended, is drawn down and with it the lateral slips which continue over the distal joint; the latter are thus brought as far distally as possible and prevented from retracting. The best relaxation of the lateral slips is obtained when the proximal joint is *fully* flexed. But to maintain full flexion of this joint is impossible without extensive splinting of the hand, and undesirable because of subsequent joint stiffness, particularly in the elderly. For these reasons we usually aim to splint the proximal joint at 90° flexion and the distal joint in hyperextension.

To apply a plaster which will maintain this position in a patient with thick stubby fingers is *not* easy. A thin felt pad is applied over the pulp and another over the dorsum of the distal end of the middle phalanx to cushion the pressure points. Plaster is applied over the finger and allowed to set while the position is maintained either by the patient himself pressing the pulp against the thumb of the same hand, or preferably by the doctor. The patient does not press firmly enough nor does he provide pressure over the dorsum of the middle phalanx. Even with experience the proximal joint often ends up flexed less than 90°, and in this position there is little better relaxation of the lateral slips than if the finger is splinted in the old-fashioned straight position with hyperextension of the distal joint. Transfixion of the phalanges by a Kirschner wire as a method of splintage is not recommended.

Splintage must be maintained for five weeks. The immediate result is often disappointing in that the deformity recurs to some extent. But the patient can be reassured; in the course of a year or so the tenuous junction appears to contract and almost full extension returns.

In a few cases relapse is complete in spite of the most careful splintage. In these and in neglected cases, *if* the symptoms warrant it (and in many people a mallet finger is a trivial disability) open repair of the tendon or arthrodesis of the terminal joint is indicated. For this, surgical aid must be sought. Indeed, unless the practitioner is adept at plaster work he may feel well advised to make his orthopædic colleagues accept responsibility from the beginning.

T. J. FAIRBANK, M.B., F.R.C.S.
Surgeon, Orthopædic and Fracture Department, United Cambridge Hospitals.

NOTES AND QUERIES

Vaccination Immunity in Infancy

QUERY (from a reader in Pakistan).—A boy, aged 4½, has been vaccinated six times, the first being at the age of two months and the last time one month ago. On each occasion he has given the revaccination reaction, i.e. vesicles after forty-eight hours, which then regressed. Pustules on the tenth day have never occurred. His mother was vaccinated at the beginning of the fifth month of pregnancy, but this also occurred with other children in the family who gave a typical primary reaction when first vaccinated. The potency of the vaccine, whether English or Pakistani, has been proved on each occasion.

May this child be regarded as immune, or should we continue trying until he produces the normal primary reaction of pustule formation? As there is a smallpox epidemic here, and it is endemic anyway, it is a matter of some concern to his parents.

REPLY.—This history suggests an immune reaction, but it is impossible to be dogmatic. My colleague, Professor Maitland, who is Professor of Bacteriology in the University of Manchester, recommends that the boy be revaccinated and, if the result is as before, bled three weeks later and the serum tested for complement fixing and neutralizing antibodies. If these are present, they would provide supplementary evidence of immunity. If there are none present, vaccination should be repeated until a normal reaction occurs

PROFESSOR WILFRID GAISFORD, M.D., M.SC., F.R.C.P.

Persistent Nasal Discharge

QUERY.—A boy of 18 months has a persistent nasal discharge. It began last November when the child's brothers brought home coughs and colds from school. At first the discharge was purulent; it then became clear mucoid. With repeated infections during the winter it became purulent and clear again on several occasions, but always persisting and sometimes accompanied by a cough. At the moment, after a seaside holiday, the discharge consists of a stream of clear mucus. There is an occasional cough which seems to be due to an excess of mucus, as once this is clear the cough does not persist. The child has remained in good spirits and appears unaffected systemically, but one feels that the next 'cold' that comes along will again produce the purulent discharge. A variety of antibiotics have been used—penicillin and 'achromycin' by mouth and 'sulfex' locally.

The points that arise are:—Is there a focus of infection? The nose appears clear but the sinuses have not been x-rayed. Is there any point in persisting with treatment? Finally, as the grandfather has asthma and an aunt has eczema, is this child likely to develop asthma as a result of sensitization to repeated infection?

REPLY.—The important point about this child's nasal discharge is its persistence. From the fact that it did not start until nearly one year of age, and as it apparently comes from both nostrils, rare congenital defects such as choanal atresia can be excluded. The discharge, although in the first instance purulent, is for the most part clear. This, with a family history of both asthma and eczema, strongly suggests an allergic cause—vasomotor rhinitis. If this is the case, examination of the nasal mucosa (with an electric auriscope) will show pale œdematous mucosa; further confirmation may be obtained by finding a high percentage of eosinophil cells in the nasal secretion at a time when the discharge is not purulent. The swollen nasal mucosa hinders drainage, so that such patients are more than usually liable to respiratory infection. In addition, the secretion of mucus causes an irritating cough.

An attempt should be made to find offending allergens. These are most likely to be house dust, feathers, orris (from face powder), and the emanations from household pets. Skin tests might reveal the causative agent but, even if these are negative, steps should be taken to avoid contact with the above as far as possible. The nasal airway may be cleared by the use of 0.5% ephedrine in saline, or of one of the phenylephrine nasal drops. These should be used sparingly, and for not more than a few days at a time, preferably when another member of the household has a cold. The use of antibiotics, either locally or systemically, should be avoided, unless infection more serious than the usual cold develops. The question of allergy to bacteria is a much debated point. It is doubtful whether such is the case in a young child, but every effort should be made to avoid the risk of producing resistant strains of organisms by indiscriminate use of antibiotics.

There is certainly a definite chance that this child may develop asthma later, a chance which makes the search for, and elimination of, any offending allergen important.

H. EVERLEY JONES, O.B.E., M.B., F.R.C.P.

Effects of Overdosage of Vitamin K

QUERY.—What toxic effects result from overdosage of vitamin K, or its synthetic analogues? What is the toxic dose for (a) adults, (b) children?

REPLY.—There is evidence that in large doses vitamin K analogues can act as hæmolytic agents. The practical clinical importance of this concerns the use of the vitamin to prevent bleeding associated with hypoprothrombinæmia in premature babies. In many centres a water-soluble analogue is routinely injected into all such infants after birth. Premature babies normally develop a raised plasma bilirubin level about the fifth day of life and the excessive administration of vitamin K can raise this level to over 18 mg. per 100 ml. and so precipitate the development of the kernicterus of prematurity. It is recommended that not more than one dose of 0.5 to 1 mg. of vitamin K should be given to premature infants as this is quite as effective in preventing postnatal hypoprothrombinæmia as larger doses.

There is no evidence of toxic effects of overdosage with vitamin K in either children or in adults.

JAMES INNES, M.D., F.R.C.P.ED.

Tuberculosis and Pleural Effusion

QUERY (from a reader in Natal).—How can one determine if a pleural effusion is caused by tuberculosis? On what criteria is it justifiable to assume that the effusion is tuberculous in origin, and therefore to start treatment with tuberculostatic drugs? The absolute diagnosis is to isolate the bacillus from the fluid but this may take six weeks and I believe that it is isolated in less than 50% of cases of tuberculous effusion.

REPLY.—It is unusual in tuberculous pleural effusion for the bacilli to be seen on examination of a straight smear; by culture methods or inoculation of a guinea-pig the number of positives obtained may approach 50%. A negative result never excludes the diagnosis. A serous lymphocytic effusion, sterile for pyogenic organisms, with no visible parenchymatous disease on x-ray should, in a young person, be regarded as tuberculous unless there is good evidence to the contrary; in older subjects malignancy must always be carefully considered. A third condition which enters into the differential diagnosis is pneumonia with an overlying serous exudate.

The distinction between these three disorders rests upon evidence derived from several sources: age, mode of onset, physical examination, study of temperature chart, x-ray and sputum tests, in addition to complete examination of the fluid. If there are good grounds for excluding carcinoma and pneumonia the patient should be treated for tuberculosis.

In opposition to what was at one time believed, the modern view is that there is no contraindication to the use of anti-tuberculous chemotherapy, but every reason to employ it. It shortens the acute phase of the illness and has reduced the incidence of later manifestations of tuberculosis from 20 or 30% to under 5%. Streptomycin, 1 g. daily, *plus* isoniazid, 100 mg. three times a day, is a useful combination with which to begin; this can be changed later to PAS, 4 g. thrice daily, *plus* isoniazid, 100 mg. thrice daily, by mouth. Treatment should be maintained for at least six months and possibly for twelve.

N. LLOYD RUSBY, D.M., F.R.C.P.

Inheritance of Buerger's Disease

QUERY.—A man, aged 30, suffers from Buerger's disease. Sympathectomy has improved his arterial troubles but he suffers from attacks of superficial migrating thrombophlebitis. His father, paternal grandfather, and one of his father's two brothers are said to have suffered similarly and have died in early middle age from vascular disease. The patient is considering marriage, but he is anxious about the prospects of his sons being affected. He is a devout Catholic. Buerger's disease is described in standard texts as being non-familial. What advice should I give this patient as to the likelihood of having affected sons?

REPLY.—This is one of those questions which it is extremely difficult to answer. As the reader says, Buerger's disease is not usually familial. Nevertheless, in this particular family there appears to be good evidence of a familial tendency, and it would clearly be wrong to tell the patient that his sons would not have a greater chance of being affected than the general population. What this chance is, no one can say but, if the family history is to be believed, the responsible gene must have a very high penetrance.

RONALD BODLEY SCOTT, D.M., F.R.C.P.

Treatment of Frigidity

QUERY.—I would be grateful for some information about 'yobinol'. I understand that it is an aphrodisiac. Is it suitable for use in women who complain of lack of interest or dislike of intercourse? I see a number of such women at a family planning clinic from time to time, and they present a problem when there is no obvious need for psychiatric treatment.

REPLY.—'Yobinol' is a preparation containing 1/20 grain (3 mg.) of yohimbine hydrochloride. In small quantities, this substance is said to dilate the vessels of the skin and of the genital organs, the latter action being the pharmacological basis for its use as an aphrodisiac. Such use, however, has now become very rare since it has been increasingly recognized that yohimbine is of little or no value in cases of sexual aversion or frigidity. Some patients may show a useful

response to methyltestosterone, given in a dose of 5 to 10 mg. sublingually; this should not be continued for more than three or four weeks at a time, with intervals of two or three weeks between courses, as otherwise virilizing effects may appear.

The fact is, of course, that most women who complain of lack of interest or dislike of intercourse are in need of psychotherapy, even if only of the 'common sense' variety. It is the minority who can be helped by drugs and, I should have thought, few if any by yohimbine.

G. I. M. SWYER, D.M., M.R.C.P.

Pigmented Moles in Childhood

QUERY (from a reader in Pakistan).—A girl, aged 6, has numerous flat 'moles'. A month ago a small one, 2 mm. in diameter, beside the right scapula became slightly raised and the surface whitish. During the last month a ring of depigmentation (1 cm. in diameter) has occurred round it, although the 'mole' itself does not appear to have altered in size. Does this mean subcutaneous extension of the 'mole' and is there any possibility of its being malignant in character? If so, what ought to be done?

REPLY.—Depigmentation is quite often seen at the periphery of innocent pigmented moles. In a child aged 6 the risk of malignancy where there are multiple lesions is regarded as negligible. No treatment is indicated.

P. B. MUMFORD, M.D., F.R.C.P.

Chronic Urethral Discharge

QUERY (from a reader in East Africa).—A healthy-looking young man has come to me for advice and treatment for a chronic urethral discharge which he has had for the past five months. The history dates from five months ago when he contracted gonorrhœa. This, he stated, was treated by a private general practitioner with two injections, presumably penicillin. Two weeks later he noticed that the profuse discharge which he had before the treatment had become less, but persisted for another three weeks, and he decided to consult another doctor who gave him a course of four injections which he thinks were penicillin injections, but without success. The discharge appears only in the mornings and a film of this examined under a microscope showed many pus cells and a few epithelial cells. No gonococci were seen.

What is the treatment of this condition, and what is the likelihood of his developing a urethral stricture?

REPLY.—The probability is that this patient contracted two infections: namely, gonorrhœa and non-gonococcal urethritis — sometimes called 'non-specific urethritis'. The penicillin may well have cured his gonorrhœa but the non-gonococcal infection remains. A fresh specimen of urethral pus should be examined for the presence of *Trichomonas vaginalis* and, if possible, the pus should be cultured for the presence of other organisms. Assuming negative findings, the patient should be treated for non-specific urethritis. Tetracycline, or oxytetracycline, by mouth is effective in most cases. A satisfactory course is to give 500 mg. at once and then 250 mg. every six hours for the following five days: that is to say twenty doses, and 5.5 grammes, in all. This is likely to clear up the discharge, and the patient's prostatic fluid should then be examined microscopically for evidence of chronic prostatitis. This is most likely to be present and, if so, the question of further treatment with prostatic massage, and perhaps more tetracycline drugs, should be considered.

Stricture formation is most unlikely unless there has been some mechanical interference with the urethral mucosa, as with irrigations which were too hot or with too strong antiseptic, or the passage of instruments in the presence of infection.

AMBROSE KING, F.R.C.S.

PRACTICAL NOTES

Leg Cramps in Pregnancy

CONSIDERABLE doubt exists concerning the etiology of the leg cramp syndrome which occurs during pregnancy—usually between the twenty-fourth and thirty-sixth weeks. In the belief that it was due to neuromuscular instability resulting from a relative calcium deficiency enhanced by an excessive intake of phosphorus, various observers have recommended treatment by means of reduction of milk intake, the administration of phosphorus-free calcium salts (e.g. calcium lactate) and/or the absorption of phosphorus from the gastro-intestinal tract with aluminium hydroxide. According to J. Abrams and G. E. Aponte (*American Journal of Obstetrics and Gynecology*, August 1958, **76**, 432), however, the pregnant woman who experiences leg cramps shows no evidence of increased neuromuscular instability. Neither could they find any evidence to support the contention that increased ingestion of dairy products predisposed to the occurrence of leg cramps. Further, in their investigation calcium lactate was no more

effective than dicalcium phosphate in the prevention and alleviation of such cramps. They contend that 'pregnant women should continue to consume foods rich in calcium and phosphorus despite the presence of leg cramps' and stress that 'the presence of leg cramps should not interfere with a well-balanced dietary intake'.

Iron for the Elderly

BECAUSE of the tendency for iron salts to produce constipation and mild abdominal cramp in the elderly, L. A. Pegel, Jr. (*Journal of the American Geriatrics Society*, August 1958, **6,** 621) has investigated the value of administering iron by means of sustained-release capsules. Each of these capsules contains 150 mg. of exsiccated ferrous sulphate in the form of multiple small coated pellets, which is said to keep the iron in the active ferrous form and to ensure its slow release throughout the intestine, thus reducing the risk of irritation. Ten patients—one man aged 64, and nine women aged 72 to 97—were given one of these capsules daily: for forty-nine days in the case of the women and for sixty days in the case of the man. Before treatment was started the hæmoglobin levels ranged from 7.5 to 11.5 g. per 100 ml. (average 9.2 g.). Following treatment, in eight of the patients the hæmoglobin rose to within normal limits, the increases varying from 0.5 to 6 g. per 100 ml. (average 2.6 g.), and the final range being 10 to 14.5 g. per 100 ml. (average 11.8 g.). There were no side-effects although all the patients had been constipated or had abdominal cramps during previous treatment with conventional iron preparations.

Warfarin

'WARFARIN sodium possesses modest advantages over dicoumarol as an anticoagulant', according to H. G. Danford and his colleagues (*Proceedings of the Staff Meetings of the Mayo Clinic*, July 9, 1958, **33,** 359) as a result of their experience with 170 patients to whom the drug was administered orally. The control group consisted of 110 patients treated with dicoumarol. The initial dose of warfarin sodium was 40 to 60 mg., and the daily maintenance dose ranged from 0 to 20 mg., usually 5 to 10 mg. Approximately 45% of the patients in each group had prothrombin activities of 30% or less in twelve to twenty-four hours. On the other hand, only 14% of the warfarin patients, compared with 24% of the dicoumarol patients, showed a prothrombin activity of less than 10% of normal at some time during the first seventy-two hours. Escape from the therapeutic range of hypoprothrombinæmia occurred in 5% of the total days of treatment in the case of warfarin and in 9% in the case of dicoumarol. With warfarin, the incidence of bleeding was comparable to that with dicoumarol, and vitamin K_1 was an efficient antidote. No other untoward effects were observed. Approximately three-fourths of the patients had normal prothrombin activity within five days of discontinuing warfarin.

The Broken Needle

ADVICE concerning the prevention, and management, of the broken needle is provided by W. Fraser-Moodie (*British Dental Journal*, August 5, 1958, **105,** 79), based upon a study of 26 cases referred to a general hospital. As the commonest cause of breakage is the use of an old needle or one that has been bent and then straightened again, no needle should be used more than six times and, if a needle is bent, it should be discarded forthwith. When giving an injection, such as a local anæsthetic, the needle should never be buried up to the hub: at least a quarter of an inch (6 mm.) should be unburied at the maximum depth of injection. The syringe should be kept absolutely steady and adequately supported, so that it is never possible for it to sway unexpectedly with the needle firmly embedded in the tissues.

Once the needle is broken, the fragments must be removed at the earliest opportunity. It is 'very unwise to leave any fragment of needle in any area around the oral cavity'. If a portion of the needle is protruding from the tissues this should be grasped at once—preferably with a small curved mosquito artery forceps if these are available, but usually only tweezers are to hand on these occasions. Action must be quick and immediate, as there is usually only about five to seven seconds to spare before the protruding end disappears. Once grasped, the fragment should be removed carefully along the same line as that occupied by the syringe during the injection. If the end is not protruding, a short incision is made over the site of the puncture under local anæsthesia, and an attempt made to locate and grasp the fragment. If this fails after a few minutes the attempt is abandoned, the incision closed by a suture, the patient told what has happened and then referred to hospital, preferably within forty-eight hours.

Bronchial Carcinoma in Young Adults

DURING the period, March 1955 to July 1957, five young soldiers (aged 18, 19, 20, 21, and 25) with primary bronchial carcinoma were investigated at the Connaught Hospital. In reporting these cases, S. E. Large and W. K. C.

Morgan (*British Journal of Tuberculosis and Diseases of the Chest*, July 1958, **52,** 185) note that two were discovered by mass radiography, neither of whom had any symptoms initially. Two complained of cough, sputum and hæmoptysis, whilst the fifth presented with headache and vomiting due to metastases. The diagnosis was finally established by bronchoscopy in two cases, lymph-gland biopsy in one, thoracotomy in one, and needle-biopsy of the growth in one. In two of the patients the diagnosis was 'unnecessarily delayed by a too ready assumption that their lesions were tuberculous'. Nevertheless, the average time elapsing between the onset of symptoms and diagnosis was under two months. Only two cases were judged operable and they survived operation (lobectomy and pneumonectomy respectively) by only six months. Two patients had deep x-ray therapy: one after a course of mustine, and one as a post-operative measure. In those not operated on the disease pursued a rapid course: one lived seventeen days from the onset of his first symptoms, one three months, and one five months.

Supplementation of Regional Anæsthesia

A MIXTURE of pethidine and promazine has been found to be 'uniformly satisfactory' by Mark Swerdlow and E. C. Cockings (*British Journal of Anæsthesia*, August 1958, **30,** 375) as a means of rendering the patient lightly unconscious while being operated on under regional anæsthesia. In 75 cases, mainly elderly men undergoing genito-urinary operations under spinal, epidural, caudal, or refrigeration analgesia or under local block, the patients were premedicated with 8 to 11 mg. of morphine and 0.64 mg. of atropine given subcutaneously about one hour before operation. Originally, promazine alone was then given, but this potentiated the morphine of the premedication, and when a fifty-fifty mixture of promazine and pethidine was tried there was often prolonged postoperative sleepiness. The most satisfactory mixture was found to be one containing a 2:1 proportion of pethidine and promazine—25 mg. of pethidine and 12.5 mg. of promazine in each millilitre. Dosage was one to four millilitres, 1 or 2 ml. being given before the regional block was performed and a further dose (or doses) after completion of the block. This 'consistently produces sleep but prolonged postoperative drowsiness is avoided'. The patient retains control of upper respiratory reflexes, maintains his own airway, and the skin is 'warm, pink and dry'. 'Care must be taken to avoid sudden movement, tilting or rough handling lest a marked fall in blood pressure result. If blood loss occurs during operation, it should be replaced at once. It is important that the regional analgesia should adequately cover the field of operation'. After operation patients are cooperative and there is usually amnesia for the whole, or a large part, of the operative period and sometimes even for the regional block.

Calcium Calculi

As a result of an investigation of 344 patients with calcium calculi of renal origin, A. Hodgkinson and L. N. Pyrah (*British Journal of Surgery*, July 1958, **46,** 10) conclude that 'a high urinary excretion of calcium does not, by itself, result in stone formation, but it increases the chance that stone formation will occur, and it appears to influence the type of stone formed'. The normal range for the urinary excretion of calcium by adults on a normal diet was 100 to 300 mg. a day for men and 100 to 250 mg. a day for women. Approximately two-thirds of the patients with stones had average urinary calcium values within or below this normal range. Conversely, approximately 8% of normal adults were found to have urinary calcium values greater than 300 mg. a day for men and 250 mg. a day for women, whereas the incidence of calcium calculi of renal origin in the general population is probably less than 0.2%. The incidence of high urinary calcium values in patients with a history of recumbency at some time in the past, a family history of stone, or an anatomical abnormality of the kidneys was approximately the same as that in calculus patients as a whole. Parathyroid adenoma or hypertrophy was found at neck exploration in 2.3% of the patients in this series. The urinary excretion of inorganic phosphorus by calculus patients did not differ appreciably from that of normal individuals.

Treatment of Nickel Poisoning

As a result of experimental work in animals and experience in 11 cases of poisoning in man, F. W. Sunderman and F. W. Sunderman, Jr. (*American Journal of The Medical Sciences*, July 1958, **236,** 26) consider that sodium diethyldithiocarbamate (dithiocarb) is an effective preparation for the treatment of nickel carbonyl poisoning. All the patients made uneventful and complete recoveries and were able to return to work within two to three weeks. They contrast these results with those in a previous series of 31 cases treated with dimercaprol, two of whom died and in the majority of those who recovered 'convalescence required several months'. It is further reported that the side-effects of dithiocarb are much fewer than with dimercaprol. The dosage of dithiocarb is based upon the

concentration of nickel in the initial eight-hour collection of urine. If the concentration of nickel is between 10 mcg. and 50 mcg. per 100 ml., dithiocarb is administered orally in doses of 0.5 g. three or four times daily, with 0.5 g. of sodium bicarbonate, in a glass of water. This is continued until the patient is symptom free and the urinary concentration of nickel is less than 10 mcg. per 100 ml. If the urinary nickel exceeds 50 mcg. per 100 ml. the same dosage is given orally or, if the patient's condition is critical, it may be given parenterally in an initial dose of 25 mg. per kg. of body weight, the total amount for the twenty-four hours not exceeding 100 mg. per kg. of body weight. The authors state, however, that they have never given it parenterally. Alcoholic drinks should be prohibited while the patient is taking dithiocarb, as there is some evidence that in such circumstances the latter has an 'antabuse'-like effect.

Treatment of Dandruff

As a result of a study of three different methods of treating dandruff, carried out on 102 patients, in which he compared salicylic acid lotion, selenium sulphide, and a proprietary preparation containing benzalkonium chloride, A. P. Caspers (*Canadian Medical Association Journal*, July 15, 1958, **79,** 113) concludes that the third of these is 'not only the most effective but also the most æsthetically acceptable, of the three preparations evaluated'. Of the thirty men in the group treated with the benzalkonium preparation, 50% responded rapidly, 46.6% moderately, and 3.3% slowly. Of the four women, two responded rapidly and two moderately. The one slight disadvantage of this preparation is its liability to cause a low-grade conjunctivitis if it gets into the eyes. In using the benzalkonium preparation, the hair is first wetted thoroughly and then the solution is well massaged into the scalp for two or three minutes. The hair is then rinsed, another lot of the preparation applied, and then the hair finally rinsed. As dandruff is liable to become worse after a visit to the hairdresser, it is recommended that the hair should be shampooed with the benzalkonium preparation as soon as possible after the visit—preferably within twelve to twenty-four hours.

Nylon Brushes and Hairfall

NYLON hairbrushes were found to be the cause of some puzzling cases of hairfall by Agnes Savill (*British Journal of Dermatology*, August-September 1958, **70,** 296). A typical case was that of a young man aged 27 who, apart from the usual retreating hairline on both temples, had 'a large, almost bald region of a triangular shape on the right side of the vertex' which had steadily enlarged during the past year. Microscopical examination revealed a condition which resembled tricorrhexis nodosa. Treatment with oil and massage was instituted but there was no sign of regrowth of hair. Upon inquiry it was found that the patient had been using a nylon hairbrush for over a year and had applied it with special vigour along the right side of the vertex. He was instructed to get a bristle brush at once, and three months later the area 'was covered with strong hair of normal length and appearance'. Investigation revealed that in many patients using nylon hairbrushes the hairs were not broken but had been pulled out with the roots. Tests were carried out with the various types of nylon bristle used for hairbrushes, and only one type, which when examined under a magnifying glass was found to have rounded points like the head of a match, was safe to use.

A Nylon Stretcher

DETAILS of a nylon stretcher, now in use at the Royal Victorian Hospital, Belfast, which allows bedridden patients to enjoy the comfort of immersion in a bath, are given by Miss Elizabeth R. Allen (*Nursing Times*, August 29, 1958, **54,** 1010). Two types of nylon have been found satisfactory: (a) what is known technically as a 'fancy cloth', 60 denier nylon, three float mock line weave on 12 ends and six picks, with 128 by 98 ends for 36-inch width; (b) a plain cloth, 60 denier nylon, ordinary weave with 104 by 104 ends for 36-inch width. The amount required for one stretcher is: 6 yards in 36-inch width, or 5 yards in 39-inch width, or 2 yards in 54-inch width. By using the material two-ply the stretcher is strong enough for lifting patients of 'full average weight'. The finished measurements are 5 feet 10 inches by 2 feet 3 inches. At five suitably spaced places the two-ply stretcher is reinforced by cross-strips of two-ply material, each strip 5 inches in width. There are five handles on each side, made from double-twisted nylon found by taking a strip from the edge of the material when cutting out. Each handle is attached to the site where the nylon is four-ply: i.e., where the stretcher is reinforced by the cross-strips.

The advantages of the stretcher are as follows: (i) It is light-weight, easily disinfected and dried following use. (ii) It is easily placed under the bedridden patient. (iii) It is comfortable for the patient to lie on in the bath. (iv) Because of its size and the type of material, the act of lifting the patient from the bath so tightens and presses the stretcher against the patient as to expel all the water, thus avoiding the wet pools so often found in the bed when a canvas stretcher was used.

REVIEWS OF BOOKS

An Introduction to Surgery. Edited by D. H. PATEY, M.S., F.R.C.S. London: Lloyd-Luke (Medical Books) Ltd., 1958. Pp. xii and 228. Figures 54. Price: Cloth 17*s.* 6*d.*; students' edition, paper covered, 9*s.* 6*d.*

PROFESSOR PATEY'S aim in this book has been to provide a simple manual to which the student can turn for guidance during the introductory period that now intervenes between the premedical instruction in the basic sciences, and the clinical work in the wards that he will shortly undertake. The aim of such a course is to familiarize him with the new tools of investigation that he will be handling; with the general principles underlying the reactions of the body to disease and injury, with the methods of examination used in clinical work, and with the practical procedures used in treatment.

This book fulfils such a purpose admirably. The writing is clear. The diagrams, so essential to one trying to master a new subject for the first time, are just right—indeed, some of the chapters, such as that on metabolic problems, would be stiff reading without them. The chapters on shock seems to hover between the shock of Baylis and Cannon in the 1914-18 War and the shock of Blalock and Buttle in the 1939-45 War. Is hæmoconcentration ever seen in shock apart from that of burns?

The book concludes with three practical sections that will ensure its popularity among students: an account of the technical procedures that are likely to be met in the wards and casualty departments, a glossary of words and terms used in surgery, and an appendix giving the normal values of substances found under normal or pathological conditions in body fluids.

The publishers have produced a volume which is not merely attractive to look at, but portable. Further they have performed a notable service to the young and impecunious public waiting for this book, by producing it in a cheaper edition which, apart from its binding, is identical with the standard edition.

Metabolic Disturbances in Clinical Medicine. Edited by G. A. SMART, M.D., F.R.C.P. London: J. & A. Churchill Ltd., 1958. Pp. vii and 358. Figures 35. Price 45*s.*

THE author has made a useful addition to the literature on the general metabolic aspects of disease, treating the subject rather in the light of the disturbances in metabolism which accompany diseases in general rather than as in the more stereotyped descriptions of metabolic diseases as such, e.g. diabetes, gout.

He has thus assembled contributors to deal with the nutritional changes in obesity, observations of fluid balance and electrolyte stability in surgical and medical conditions. A chapter is devoted to the information accumulated in recent years on the effect of injury and operation on metabolic processes. The newer views on the production of liver histopathology are well expounded and urinary amino-acid loss is illustrated by chromatographic studies. There is an excellent chapter on the metabolic diseases of bone, including hyperthyroidism, renal rickets and osteomalacia. The section dealing with the hæmatopoietic system contains detailed reviews of iron metabolism, and porphyrin synthesis and abnormalities in production of hæmoglobin and blood proteins. Myelomatosis is dealt with in this connextion. The megaloblastic anæmias are considered in detail. Under the heading of the central nervous system are included a number of diverse conditions including spontaneous hypoglycæmia, neuronal lipoidosis, and myasthenia gravis.

The book covers a wide range of metabolic abnormality. Notable omissions are, for example, anorexia nervosa and certain of the hereditary anomalies like cysturia. But in spite of such exceptions the author has produced a readable addition to the present literature on this aspect of medicine.

Modern Trends in Anæsthesia. Edited by FRANKIS T. EVANS, M.B., F.F.A.R.C.S., and T. CECIL GRAY, M.D., F.F.A.R.C.S. London: Butterworth & Co. (Publishers) Ltd., 1958. Pp. ix and 331. Figures 30. Price 67*s.* 6*d.*

THE avowed aim of the editors of this book was the commendable one of presenting a collection of authoritative reviews covering new knowledge in a wide range of the scientific and clinical aspects of anæsthetic practice. An excellent selection of subjects of current interest and importance has been made and entrusted to an international team of research workers and clinicians. Some of the twenty-two contributors have sustained the editorial ambition and hopes by providing sound discriminating appraisals of recent developments and the directions in which the latter may be heading but others have merely catalogued, sometimes in stilted fashion, the work in progress along with much that is not so new. There is considerable variation

therefore in the quality of the chapters, ranging from excellent to only fair.

The opening chapter on relaxants sets a good example of how the main purpose of a review lies not in laborious abstraction of all that has been published on a particular subject but in expert selection and assessment of such new work as is likely to prove of value in the future. Appropriate to the increasing activities and responsibilities of anæsthetists is the inclusion of helpful, forward-looking discussions of conceptions of consciousness, the pituitary-adrenal axis, hypothermia, pulmonary ventilation and its control, analgesia and sedation, anæsthesia and disease, and regional anæsthesia in anæsthetic practice and therapeutics. In its format and general production this volume is pleasing and of a high standard and despite the inequalities mentioned it can be commended.

Abnormal Labor. By L. A. CALKINS, M.D. Springfield, Illinois: Charles C Thomas; Oxford: Blackwell Scientific Publications, 1958. Pp. vii and 70. Figures 6. Price 21*s.*

THIS readable little monograph is full of practical common-sense advice. The subject of abnormal labour is discussed concisely in less than 50 pages whilst the remainder deal with predicting the duration of the second stage of labour. This is a subject which has been extensively studied by the author and his clinical experience is carefully presented. The emphasis throughout is on the need for accurate clinical observation with its corollary of hours spent, when necessary, by the bedside of the labouring woman. The author is a strong advocate of the 'pitocin' drip in circumstances which he clearly defines in relation to all three stages of labour. The safeguard of constant attendance at the bedside when oxytocics are given intravenously is stressed repeatedly. The clinical significance of the 'firm cervix' is discussed in some detail and the advice given that every labour should be assessed by a specialist if full dilatation has not occurred after 16 hours, or if the second stage lasts more than 30 minutes. Vaginal examination is preferred to rectal. Conventional terminology is sometimes used loosely and references are made to transverse and occiput 'presentations', but the meaning is always clear. This little book is good value for a guinea.

Pediatric Index. By EDWIN F. PATTON, M.D. London: Henry Kimpton, 1958. Pp. 639. Price £5 1*s.* 6*d.*

THIS book is subtitled 'A Guide to Symptomatological Diagnosis and Current Management'. It is intended to be used by the doctor with a diagnostic problem. He looks up the chief complaints in the first part of the book and having found the description which best fits the situation he then looks up the presumptive diagnosis in the second part, takes steps as set out to establish a definite diagnosis and applies appropriate treatment. Special information (doses and so forth) and special methods are summarized in the last sixteen pages. The book represents an enormous amount of work, but it is not nearly so compact as Wilburt Davison's 'The Compleat Pediatrician' to which it is an obvious rival. It is difficult to assess its value. For those who like this sort of approach in medicine it will have some appeal.

Care of the Premature Infant. By EVELYN C. LUNDEEN, R.N., and RALPH H. KUNDSTADTER, M.D., F.A.C.P., F.A.A.P. London: Pitman Medical Publishing Co. Ltd., 1958. Pp. xv and 367. Figures 87. Price 60*s.*

THIS is an up-to-date account of the procedures at the well-known 'premature infant station' at Michael Reese Hospital, Chicago. The late Dr. Julius Hess together with Miss Lundeen wrote a classic on 'The Premature Infant' and the present volume is essentially a modernized version with Dr. Kundstadter taking over responsibility for the medical side. It gives an excellent account of many aspects of the problems presented by the prematurely born infant, and of particular interest are the measures described for home care and follow-up and the city-wide plan for dealing with prematurity as a serious menace to child health. The book is well illustrated and, whilst some difference of opinion could be expressed on details, the advice given is fundamentally sound—tested, as Miss Lundeen states, for over twenty-five years. The price of the volume in this country seems high.

External Collimation Detection of Intracranial Neoplasia with Unstable Nuclides. By G. M. SHY, M.D., M.R.C.P., R. B. BRADLEY, B.S., and W. B. MATTHEWS, Jr., B.S., *et al.*. Edinburgh: E. & S. Livingstone Ltd., 1958. Pp. vii and 144. Illustrated. Price 30*s.*

THE introduction of radioactive isotopes has opened up wide fields of investigation and of treatment. It is natural that attention should have been directed to the possibility of devising a method whereby the selective uptake of a radioactive substance by a focal brain lesion could be demonstrated graphically. Provided the substance was harmless in the dose given accurate topographical diagnosis would be available with no risk to the patient. In this book a brief account is given of the development of

such methods. In recent years the authors have evolved apparatus with which many of the earlier difficulties have been overcome. The collimator is the heavy-metal, cone-shaped end-piece of the apparatus which abuts on the patient's head, and through which the gamma rays pass to the scintillation detector. The book includes reproductions of scans of cases of glioma, metastases (single and multiple) acoustic tumour, granuloma, vascular hamartoma and carotid thrombosis. Some of the illustrations are quite dramatic, particularly in a patient with multiple cerebral metastases, in which the two lesions are quite clearly depicted.

The authors say that so far in their hands, the method has given an accuracy of diagnosis of an abnormality of about 85 per cent. It is difficult to predict whether this diagnostic method will in time oust the firmly established procedures of angiography and ventriculography. The apparatus at present is bulky and extremely expensive, and this latter factor alone will strictly limit its adoption. The same criticism, however, was doubtless levelled against Röntgen's apparatus when it was first introduced. But the combination of a diagnostic method of this kind in association with a means of attracting therapeutic radioactive applications to the areas of selective take-up, would be a great advance in the treatment of irremovable gliomas. The book is well written with excellent illustrations and those interested in the highly technical physical problems will find detailed information.

The Art of Clinical Refraction. By THEODORE H. WHITTINGTON, M.D., M.R.C.P., D.O.M.S. London: Oxford University Press, 1958. Pp. xiii and 286. Figures 78. Price 30*s.*

THIS is a well-produced book in which the author is at pains to emphasize the clinical aspect, as the title suggests, and to consider the whole subject of refraction as part of the clinical investigation and, if necessary, the treatment of a patient. There is a note of simplicity throughout. Optics are mentioned only in a directly applied manner and not described as a basic subject; as a possible consequence it is doubtful whether the description of the theory of retinoscopy would be very clear to a beginner. Having described normal vision and devoted a preliminary chapter to the art and science of refraction, retinoscopy, accommodation, image formation, and the role of prisms, the author considers the investigation and treatment of patients according to their refractive errors. Binocular vision and its defects are given two chapters; details of consulting room practice another. 'The effects of lenses' is included in the chapter on prescribing and fitting. Amblyopia comes in a rather heterogeneous chapter of doubtful value; refraction work at extremes of age is discussed, and a section is given to visual aids for the partially sighted. The section on astigmatism is good in every way, and the remarks on the doctor's attitude towards cataract or its absence are excellent.

A few criticisms are inevitable. It is strange that the author should continue to refer to Jæger types—a standard now outmoded for many years. Early in the book, on page 6, he talks about eye-strain without having defined this unfortunate term. One failed to find a reference to ciliary spasm—an important factor—even in the index.

Although a lot of this book is unavoidably repetitive, it is complementary to similar treatises such as those of Goulden and Duke-Elder, and should prove valuable to a postgraduate beginner.

Breathing Exercises. By GLADYS M. STOREY, S.R.N., F.C.S.P. London: Faber & Faber LTD., 1958. Pp. 77. Figures 20. Price 8*s.* 6*d.*

THE appearance of three books on the physiotherapy of the chest within the last eighteen months points to the growing importance of the subject in this field of work. The present volume tells quite simply the methods which Miss Storey uses to overcome 'the problem which may be encountered when breathing exercises are ordered'. The first part deals with the physiological and remedial principles involved, which lead to the application of these principles to specific medical and surgical disorders. Emphasis is laid upon relaxation and the control of breathing rather than on the more strenuous approach suggested by the word *exercises*. An optimistic note is struck in the treatment of pulmonary emphysema; it is here rather than in bronchial asthma that the necessity for beginning treatment early in the disease should be made clear. Children receive individual attention in a delightful and homely manner. The closing chapter contains some of the contraindications to treatment. Twenty line illustrations add value to the text.

Scottish Social Welfare 1864—1914. By THOMAS FERGUSON. Edinburgh: E. & S. Livingstone Ltd., 1958. Pp. xi and 610. Illustrated. Price 42*s.*

THIS is a worthy successor to the author's 'The Dawn of Scottish Social Welfare'. It covers a period which witnessed a revolutionary change in social conditions in Scotland. When the book begins it deals with a country in which

sanitation in the modern sense scarcely existed, housing conditions were primitive, destitution was rife, drunkenness was a major problem and infectious diseases such as cholera and typhus were still deadly realities.

To the older generation the book will recall memories of conditions which were just disappearing into the limbo of the past in their younger days. To the younger generation it will be a salutary reminder that the 'good old days' were not so good as some have made them out to be. On the other hand, to maintain a proper sense of perspective it must be remembered that all the reports and blue books upon which this book is based were concerned merely with the seamy side of life. The reformers were much too interested in the vices and defects of the area to worry about the virtues and advantages of the times.

NEW EDITIONS

Modern Clinical Psychiatry, by Arthur P. Noyes, M.D., and Lawrence C. Kolb, M.D., fifth edition (W. B. Saunders Co., 56*s*.).—Dr. Noyes has been joined by Professor Kolb of Columbia University as co-author of this well-established American textbook. Its structure is substantially unchanged and the subject-matter has been kept well up-to-date. There are two new chapters: one (14 pp.) on pharmacological therapy referring especially to the main groups of tranquillizing drugs, and one (12 pp.) on psychiatry and the law (U.S.A.). These included, the book has grown by 85 pages. This is a good solid work with a predominant psychodynamic flavour. Abundant references are well chosen and there is a very full index. Although its main value will be for those who are specializing in psychiatry, it is easy to read and the interested practitioner will be able to learn much from it that will help him in his practical approach to patients.

Textbook of Gynæcology, by John I. Brewer, M.D., PH.D., second edition (Baillière, Tindall & Cox Ltd., £6).—Once more Professor Brewer of Chicago has produced a notable contribution to American gynæcological literature, and, apart perhaps from some points of emphasis, its teaching conforms closely to the best British practice. It is divided into two roughly equal parts: the first dealing mainly with the symptoms occurring in childhood, in maturity, and in advanced years; the second with a detailed description of the major entities. Throughout there is evidence of fresh and stimulating thought. Perhaps the hard core of practice is the younger woman with cyclical bleeding. The author emphasizes that knowledge is still incomplete and treatment other than radical is often unsatisfactory. Large amounts of œstrin are advised. Culdoscopy receives a favourable mention. In artificial insemination the results have been discouraging: 33% of pregnancies followed fimbrioplasty, 10% of pregnancies followed transplantation of the tubes into the uterus. These are figures substantially higher than those obtained in this country. For stress incontinence a local repair of the Kelly-Bonney type is advised. The discussion on combined radiation and surgery is outstanding and the author gives a clear account of the limiting conditions of the radium menopause.

The whole book, as well as being beautifully produced, is most complete and stimulating.

Pathology for the Physician, by William Boyd, M.D., F.R.C.P., is officially the sixth edition (Henry Kimpton, £6 6*s*.) of the textbook which, under the title of 'The Pathology of Internal Diseases' has been the great standby of so many students and postgraduates during the last quarter of a century. The new title brings it into line with the author's companion volume 'Pathology for the Surgeon'. The change of title has been accompanied by a radical rewriting. Indeed, as the author points out, in many respects this is a new book rather than a new edition. It may not be to the liking of all pathologists but for the medical student and the clinician it has the great advantage of correlating pathology with physiology, biochemistry and clinical medicine in a way that no other book does. For this reason it is certain to have an outstanding appeal. The only criticism of the new edition is the publishers' decision to set it in two-column pages. In spite of this retrograde step the book can be thoroughly recommended.

Elementary Bacteriology and Immunity for Nurses, by Stanley Marshall, M.D., (H. K. Lewis & Co. Ltd., 9*s*.).—This popular and up-to-date little book appears in its third edition and with more space devoted to the increasing number of antibiotics. The book is divided into four parts covering respectively general bacteriology, immunity, tuberculosis, and all the special tests associated with the practice of clinical bacteriology. At the end of each section there is a useful summary, and a set of questions, and some points are made clearer by being put in the form of helpful tables. This book is a *sine qua non* for nurses and students for elementary public health examinations.

The contents of the December issue, which will contain a symposium on 'Respiratory Disorders', will be found on page A 134 at the end of the advertisement section.

Notes and Preparations see page 669.
Notes from the Continent see page 673.
Fifty Years Ago see page 675.
Motoring Notes see page A 101.
Travel Notes see page A 109.
Approved Names see page A 113.

NOTES AND PREPARATIONS

NEW PREPARATIONS

'FENTAZIN' preparations contain perphenazine, a new phenothiazine derivative which is said to be five times more effective than chlorpromazine and can therefore be administered in proportionately smaller dosage. It is intended for the treatment of all types of psychiatric disturbance and is also 'a powerful anti-emetic'. Issued as tablets of 2, 4 and 8 mg., in bottles of 50 and 500, and in 1-ml. ampoules containing 5 mg. (containers of 5 ampoules). (Allen & Hanburys Ltd., Bethnal Green, London, E.2.)

'PENITRIAD' tablets each contain phenoxymethylpenicillin potassium equivalent to 60 mg. of the free acid; sulphadimidine, 167 mg.; sulphadiazine, 167 mg.; and sulphathiazole, 167 mg. They are indicated in the treatment of infections due to penicillin- and sulphonamide-sensitive organisms. In gram-negative bacillary infections due to organisms of limited sensitivity to either penicillin or sulphonamides, 'notably in respiratory tract infections associated with the presence of *Hæmophilus influenzæ*', the activity of the combination is likely to be 'appreciably greater than that of either penicillin or a sulphonamide alone'. Supplied in containers of 20 and 250. (Pharmaceutical Specialities (May & Baker) Ltd., Dagenham, Essex.)

'PREDNELAN-N' intra-articular injection contains 25 mg. of prednisolone acetate and 5 mg. of neomycin sulphate in each millilitre, and is intended for the treatment of rheumatoid arthritis, osteoarthritis, traumatic arthritis, acute gouty arthritis and bursitis. The effect is said to be more prolonged than that of an equivalent dose of hydrocortisone, lasting from a few days to a few weeks, and 'there is no lessening of effect after repeated injections'. Available in vials of 5 ml. and 1 ml., in boxes of six. (Glaxo Laboratories Ltd., Greenford, Middlesex.)

'STREPSILS' are lozenges containing 1.2 mg. of dybenal and 0.6 mg. of amyl-*meta*-cresol, and are intended for the prevention and relief of mouth and throat infections. They are said to have a wide range of activity, being lethal to many bacteria in one minute, and to be soothing, non-toxic and non-sensitizing. Supplied in vacuum tins containing 24 individually wrapped lozenges. (Boots Pure Drug Co. Ltd., Station Street, Nottingham.)

'TELMID' tablets each contain 100 mg. of dithiazanine iodide, which is a broad-spectrum anthelmintic stated to be 'highly effective' against threadworm, roundworm, whipworm and strongyloides. No fasting, special diet or other supplementary treatment is required. Available in bottles of 15 and 100 'specially coated' violet tablets. (Eli Lilly & Co. Ltd., Basingstoke, Hants.)

'ULTANDREN' tablets contain fluorohydroxymethyltestosterone, which is said to be five times more potent than methyltestosterone, both as an androgen and an anabolic agent, when taken by mouth, and therefore 'can be expected to supersede the injection and implantation of testosterone preparations'. Issued as tablets of 1 mg. or 5 mg., in containers of 25, 100 and 500. (Ciba Laboratories Ltd., Horsham, Sussex.)

PHARMACEUTICAL NOTES

ALFONAL LTD. announce the introduction of their range of dairy products containing unhydrogenated corn oil in place of milk fat, which are intended for use in those cases in which it is necessary to lower the blood cholesterol. Milk, milk powder and cheese spread are available, and also margarine in which the fat is 75% pure corn oil. (Shell-Mex House, Strand, London, W.C.2.)

GLAXO LABORATORIES LTD. announce that they are now marketing the following vaccines:—'*Hæmophilus influenzæ* vaccine (Glaxo)' for use in chronic bronchitis. This is a saline suspension of killed *Hæmophilus influenzæ* containing 1000 million bacterial cells per ml., freshly isolated from cases of chronic bronchitis during an acute exacerbation of the disease. Issued in 10-ml. vials.

'Invirin' polyvalent vaccine for immunization against the virus of influenza. The vaccine (of killed virus) is standardized to contain 20,000 hæmagglutination units per ml. comprising two parts A/Singapore/1/57, one part A/Nederland/36/56 and one part B/England/10/54. Issued in 1-ml. ampoules in boxes of six.

'Staphylococcus Toxoid B.P. (Glaxo)' for immunization against chronic staphylococcal infection. This is a purified fluid preparation derived from a potent soluble toxin of a *Staphylococcus aureus* strain, standardized to contain not less than 10 Lf per ml. Issued in 5-ml. vials. (Greenford, Middlesex.)

IMPERIAL CHEMICAL INDUSTRIES LTD. announce that 'hibitane' (chlorhexidine diacetate) concentrate 2% w/v has been replaced by a 5% w/v concentrate based on the digluconate salt. (Pharmaceuticals Division, Fulshaw Hall Wilmslow, Cheshire.)

SMITH & NEPHEW PHARMACEUTICALS LTD. announce that their calcium B.PAS/Isoniazid preparation, 'therazid', is now available in an additional strength, to be known as 'therazid forte' and containing 3.5 g. of calcium B.PAS and 87.5 mg. of isoniazid B.P. (Bessemer Road, Welwyn Garden City, Herts.)

FILM NEWS

The Management of Twins in Pregnancy and Labour (16 mm., colour, sound; running time 22 minutes) outlines a routine for the successful management of twins from antenatal care to the time of delivery and shows two complete deliveries, one with complications. It is stated that if the conditions outlined in the film are fulfilled the general postnatal requirements of a mother of twins should be no different from those of a woman with a single child.

The Routine Use of Ergometrine in the Third Stage of Labour (16 mm., colour, sound; running time 7 minutes) advances arguments in favour of the routine use of ergometrine in the third stage of labour and then gives a practical demonstration of its use.

Both these films were produced in collaboration with Professor W. C. W. Nixon, and copies are available on free loan from the Wellcome Foundation Ltd., The Wellcome Building, Euston Road, London, N.W.1.

ROYAL SOCIETY OF MEDICINE

THE next meeting of the Section of General Practice will be held at 8.15 p.m. on Wednesday, November 19, when the subject for discussion will be 'Colonic Disorders'. The opening speakers will be Dr. Kenneth Milne, Sir Ralph Marnham and Dr. J. F. Stokes.

JAMES MACKENZIE LECTURE

THE fifth James Mackenzie Lecture of the College of General Practitioners will be given by Dr. G. F. Abercrombie at 11.30 a.m. on November 22, 1958, in the Great Hall, B.M.A. House, Tavistock Square, London, W.C.1. The title of the lecture will be 'The Art of Consultation'. Visitors will be welcome.

STEPHEN PAGET MEMORIAL LECTURE

'The Irrational in Public Life' is the title of the twenty-seventh Stephen Paget Memorial Lecture organized by the Research Defence Society in its jubilee year. The lecture, which will be delivered by Mr. Richard Fort, M.P., will be given on Tuesday, November 18, 1958, in the Lecture Theatre, Zoological Society of London, Regent's Park, London, N.W.1. All members of the Society and their friends will be welcome.

LONDON MEDICAL EXHIBITION

THE London Medical Exhibition will be held in the Royal Horticultural Hall, London, S.W.1, from November 10 to 14 inclusive. It will be officially opened by Sir Gordon Cameron, F.R.C.P., F.R.S., Professor of Morbid Anatomy at University College Hospital Medical School in the University of London.

CHRISTMAS GIFTS FUND APPEAL

SIR HENRY TIDY, President of the Royal Medical Benevolent Fund, writes:—'To receive a gift at Christmas times is a joy to everyone, but particularly to those who are lonely or in need. To none is a gift more welcome than to those who have fallen on hard times. Our beneficiaries include colleagues who have met with misfortune, and widows and children who are often in desperate need when their breadwinner has been taken before he was able to make provision for them. A gift at Christmas will enable them to enjoy some of the traditional good cheer of the season'. Contributions, marked 'Christmas Gifts', should be sent to the Secretary, Royal Medical Benevolent Fund, 1 Balliol House, Manor Fields, Putney, London, S.W.15.

NAPT CHRISTMAS SEALS

THIS year the sheets of Christmas seals issued by the National Association for the Prevention of Tuberculosis take a different form and picture 100 different spring or summer flowers commonly found in Britain. The seals provide funds for the work of the Association in preventing tuberculosis, bronchitis, lung cancer and other diseases of the chest and heart. The seals, which are printed in gay, attractive colours and bear the international symbol of the double-barred red cross, can be obtained, price 4s. per 100, from the Duchess of Portland, D.B.E., Chairman, NAPT, Tavistock House North, Tavistock Square, London, W.C.1.

NUFFIELD FOUNDATION

IN March this year the Nuffield Foundation completed the fifteenth year of its existence. During this period, according to the annual report of the Foundation for the year ended March 31, 1958, the Foundation has disbursed practically £8½ million. The sum distributed during the year covered by the annual report was £850,000. The outstanding medical contribution was a grant of £80,000 for the endowment of a Chair in Children's Surgery at the Hospital for Sick Children, Great Ormond Street. The only other similar chair in the English-speaking world is at Boston, Massachusetts. Other medical grants include: £2,200 for the development of the heart-lung machine

at the London Postgraduate Medical School; £2000 for the study of artificial kidneys in the department of medicine, Leeds; £2,250 a year for three years to the Institute of Neurology, National Hospital for Nervous Diseases, for an investigation into the treatment of cerebrovascular disease; and £10,700 for an investigation into disseminated sclerosis at the United Oxford Hospitals.

FAMILY PLANNING ASSOCIATION

THE opening of 25 new branch clinics during 1957, bringing the total number in England, Scotland and Wales to 270, shows that the Association, whose annual report has just been published, have again had a very active year. A total of over 300,000 people were helped by F.P.A. services during the year, and the pregnancy laboratory dealt with about 90 cases a week. The sub-fertility unit reported 'a marked increase in the number of patients referred from hospitals and as the outcome of the growing attention being paid to this aspect of the work in the F.P.A.'s own clinics'.

LIVER DISEASE IN AFRICA

THE February to April issues of *The Leech*, the journal of the Medical Graduates Association and the Students Medical Council of the University of Witwatersrand, Johannesburg, have been combined to form a special issue devoted entirely to the proceedings of the conference on 'The Liver and its Reactions in Africa', which was held in Johannesburg in May 1957. As an authoritative review of a subject of growing importance, this combined issue can be thoroughly recommended to all concerned with African medicine.

HEALTH CENTRES

NINE health centres have been established by local health authorities since the inception of the National Health Service, according to the Parliamentary Secretary to the Ministry of Health in reply to a question in the House of Commons. Three are under construction and another will be started this year. Nine other schemes have been proposed, and three at least of these are likely to be started in 1959-60.

LAUNDERING SOILED ARTICLES

IN 1950, Lewisham introduced a scheme whereby the soiled bedding and clothing of incontinent persons could be dealt with at the Council's disinfecting station. In his annual report for 1957, Dr. E. H. R. Smithard, the medical officer of health, reviews the first seven years' working of the scheme. The total number of articles dealt with has risen from 5000 in the first year to over 41,000 in 1956. Collection of the soiled laundry is made once, or more usually twice, a week, depending upon the severity of the case, and the articles are returned the next day, or in some cases the same day. No issue of replacement articles is made, but this can often be arranged through the National Assistance Board, the Red Cross, or the W.V.S.

DOLLARS AND DRUGS

LAST year, according to *The Economist*, sales by the pharmaceutical industry in the United States rose by 15%, and totalled $1.7 billion. About two-thirds of these were dispensed on prescription. Sales of tranquillizers are still booming with an annual turnover of around $200 million. It is expected that over a period of five years this particular boom has doubled the sales of Smith Kline & French. Sales of Salk poliomyelitis vaccine have reached an annual value of $40 million. Research, of course, is the key to these tremendous sales. Pharmaceutical companies are spending about 20% of their profits before tax in research, and it is estimated that this year the research budget will exceed by 5% the record $127 million spent last year. The importance of this research drive is well exemplified by the report that products unknown ten years ago constituted 70% of the sales of Merck and Company last year.

ORAL ANTIBIOTIC FOR RINGWORM

NEW hopes for a safe and effective systemic method of treating ringworm are raised by a report by J. C. Gentles (*Nature* (*Lond.*), 1958, **182**, 476) of trials with griseofulvin, a metabolic product of several *Penicillium* species, in guinea-pigs infected experimentally with *Microsporum canis*. A highly inflammatory reaction developed in all the control animals but in none of those who received griseofulvin. Histological examination showed that in the treated group about half the hair follicles were infected after four daily doses and by the eighth daily dose infected follicles were present only very infrequently. Skin sections of the untreated controls at these times showed that almost all the hair follicles were heavily infected. It proved equally effective when given orally to guinea-pigs experimentally infected with *Trichophyton mentagrophytes*. Other workers have recorded that mammalian toxicity is low.

DEATHS FROM DENTAL ANÆSTHESIA

ACCORDING to Victor Goldman (*Brit. dent. J.*, 1958, **105**, 160), in the four-year period, 1952-55, 7,682,750 dental anæsthetics were given in this country, with 56 deaths. This gives an incidence of 0.0073 per 1000, which is described as 'one which does credit to all concerned and particu-

larly to the type of outpatient dental anæsthetic given in this country'. On the other hand, concern is expressed that 20 of the 56 deaths occurred when an intravenous barbiturate was used. If it is assumed that intravenous barbiturates were used once in fifty times (a high figure it is suggested), this means that the death rate would be 0.13 per 1000, and the corresponding rate from inhalation anæsthesia would be only 0.0048 per 1000. The comment is added: 'This gravely increased risk to life should be considered very seriously before supporting any move for the general use of intravenous barbiturates in the dental surgery for the outpatient'.

OBSTETRICAL RADIOLOGY

On the basis of experiments on mice, Dr. Howard Curtis, of the U.S. Atomic Energy Commission estimates that a pregnant mother who has an x-ray taken of her unborn child is shortening the life of the child by twelve days.

CANADIAN COMMON COLD

'From the point of view of mental hygiene, colds may provide an innocuous emotional substitute and outlet, and a legitimate excuse for regression, rest and recovery which, if physically denied, may result in worse psychic or psychosomatic damage'. Dr. Daniel Cappon (*Canad. med. Ass. J.*, 1958, **79**, 173).

PUBLICATIONS

Respiratory Disease and the General Practitioner, by C. H. C. Toussaint, M.R.C.S., L.R.C.P., D.P.H. —The general arrangement of this book remains much the same as that in the original small booklet on this subject by the same author but the sections on pulmonary tuberculosis have been expanded; there are brief accounts of bronchogenic carcinoma and bronchitis. The text suffers from being too dogmatic and tends to place too much emphasis on mass radiography (even dismissing genetic hazards of repeated exposure to x-radiation). The quality of the x-ray reproductions is excellent and the general treatment of the subject is good. (National Association for the Prevention of Tuberculosis, price 7*s.* 6*d.*)

Common Chest Conditions, by Wilfred Benson, M.D., F.R.C.P. *Cooking and Eating for Health*, by John Clyde, M.D., PH.D., B.SC., Alan Porter, M.B., CH.B., and Evelyn Rose. *It's Healthy to be Human*, by F. R. C. Casson, M.B., B.S., D.P.M.— *The Family Doctor* series of books has set a commendably high standard for books for the instruction of the lay public. The first two of these three latest additions to the series maintain this standard, but the third lapses deplorably. It presents a philosophy of life which is the antithesis of the Christian faith from which western civilization draws all its strength. (British Medical Association, price 10*s.* 6*d.* each.)

Human Dissection. Its Drama and Struggle, by A. M. Lassek, M.D., of the department of anatomy, Boston University School of Medicine, is a history of the difficulties which anatomists have encountered throughout the ages in obtaining adequate subjects for dissection. In spite of the style, which is scarcely up to Boston standards, it makes interesting reading. (Charles C Thomas; Blackwell Scientific Publications, price 50*s.*)

Nursing is the first nursing manual issued jointly by the St. John Ambulance Association, the St. Andrew's Ambulance Association and the British Red Cross Society. It provides instruction for those caring for the sick, and incorporates the training requirements of the National Hospital Service Reserve. In these days when the shortage of hospital beds and the tendency to discharge patients from hospital at an earlier stage make it necessary for many non-professional people to care for their relatives at home, this book will be of great value in helping them to acquire the skill which, 'though often a matter of common sense, must be learnt'. (Price 4*s.* 6*d.*)

Expert Committee on Water Fluoridation. First Report, WHO Technical Report Series No. 146, is a review of the available information which will convince all but the fanatic of the value and safety of this simple method of reducing the incidence of dental caries. (H.M. Stationery Office, price 1*s.* 9*d.*)

Pitman Medical Catalogue, September 1958, is a complete index of the publications of the Pitman Medical Publishing Co. Ltd., from whom copies are available. (39 Parker Street, London, W.C.2.)

OFFICIAL PUBLICATIONS

Out-patient Waiting Time. Hospital O and M Service, Report No. 1, gives the results of a study of outpatient arrangements at five hospitals and a number of clinics and is the first of a series of reports and investigations to be undertaken by the Ministry of Health's Hospital Organization and Methods Service. (H.M. Stationery Office, price 1*s.* 3*d.*)

Report on the Resettlement of Disabled Persons during the Year 1957 is a useful extract from the annual report of the Ministry of Labour and National Service for 1957. (H.M. Stationery Office.)

NOTES FROM THE CONTINENT

GERMANY

Diabetes mellitus.—A wide variety of subjects was dealt with at the Third Congress of the International Diabetes Federation, which was held in Dusseldorf this summer. Much attention was devoted to the problem of diabetic angiopathy. Mohnike noted that the younger the patient at the onset of diabetes the greater the chance of his developing peripheral vascular disease. There is also a close correlation between the severity of the disease and the incidence and the severity of the peripheral vascular lesions. Diabetics of asthenic build seem to have a more favourable prognosis than those of sthenic build. Other topics dealt with included the risk of permanent damage to the brain as a result of prolonged hypoglycæmia, and the importance of routine medical examinations as a means of detecting diabetes at an early asymptomatic stage. The oral hypoglycæmic agents naturally attracted much attention, the emphasis being laid upon their mode of action. One view put forward was that the presence of the β cells in the pancreas was essential for the drugs to be fully effective.

An interesting feature of the congress programme was the discussion on the quack remedies for the disease—a problem of no significance in the United Kingdom but one which still causes anxiety in certain continental countries. Doctors from several countries were able to report severe, and sometimes fatal, complications occurring in diabetic subjects who had relied for treatment on various—often very expensive—herbs, powders or mechanical forms of therapy. German delegates complained that sometimes even pharmaceutical firms sold such 'remedies' but, unfortunately, under the existing laws of the Republic it was impossible to prosecute such firms.

Malignant cells and irradiation.—According to O. Warburg, hydrogen peroxide is found in cells which have been irradiated. In non-malignant cells there is a catalytic enzyme which destroys hydrogen peroxide and therefore prevents it from having any deleterious effect on the cell. This enzyme is lacking in malignant cells and therefore, theoretically, such cells should be destroyed by the hydrogen peroxide (a strong cell poison) produced by irradiation. The erythrocytes, however, contain several catalysts and these tend to affect hydrogen peroxide. Warburg therefore advances the hypothesis that, if during irradiation the circulation to the irradiated area could be maintained by a fluid containing no erythrocytes, a more potent action would be obtained in the malignant cells. It would, of course, be essential to ensure that this blood substitute was adequately oxygenated. He reports that it has been demonstrated *in vitro* that pure hydrogen peroxide, without irradiation, is capable of destroying cancer cells.

Social medicine.—Under this heading may be included a number of variegated subjects which have recently been under discussion in medical circles. At the 61st 'German Doctors' Day', which was held at Garmisch-Partenkirchen, concern was expressed at the increasing publicity being given to medical matters in illustrated magazines, films, and on television—on the grounds that it pandered more to sensationalism than to a genuine interest in public health. A strong appeal was made for closer cooperation between responsible publicists and the medical profession to ensure that medical matters should be presented to the lay public in a reliable and authentic manner.

At the 1st German Hospital Day, which was held in Cologne, doctors, pharmacists, nurses and administrators met to discuss the role of the hospital in the community. Various papers stressed the importance of the hospital library as a means of relieving the monotony of hospital life and giving bedridden patients something to maintain their interest—and therefore their morale.

Figures recently issued show that, as compared with 1896, the cost of medical education has risen 300%, that of becoming established in practice 557% and practice expenses 333%, whilst there has been a corresponding rise in taxation. It is contended that the increase in payments to doctors has not risen correspondingly.

In Western Germany increasing concern is being felt—and expressed—at the effects of Eastern Germany policy on cultural and scientific contacts between the two zones. New regulations in Eastern Germany make it almost impossible for students and scientists there to attend conferences in Western Germany. One practical result of this is that since January this year 621 doctors and 166 teachers have fled from the Eastern to the Western Zone. Typical of the rigour with which the Eastern administration is dealing with the situation is the enactment that professors who flee to Western Germany shall be deprived of their academic degrees.

Genius and the brain.—Yet another attempt to correlate genius with macroscopic or microscopic changes in the brain has ended in failure. This time the basis of investigation was

the brain of Count Hermann Keyserling, the well-known author and philosopher who spoke Russian, French, English, German and Spanish with equal fluency and was equally at home with Latin and Greek. At post-mortem examination the only finding of note was an increase in the convolutions in the right side of the brain but without any definite evidence of increase in size. Equally disconcerting to those who believe that genius can be correlated with detectable physical features in the brain was the absence of any enlargement of Broca's area—an enlargement which, it has been contended, is often found in language geniuses. The author of this study concludes that genius cannot be measured physically or chemically.

ITALY

Treatment of depressive states.—Satisfactory results are reported by C. Fazio, F. Giberti and C. Loeb from the use of a new preparation, the chlorhydrate of N-(γ-dimethyl-aminopropyl)-iminobenzyl (G. 22355. Geigy), in the treatment of depressive states. Their conclusions are based upon the results obtained in a series of 50 patients (19 males and 31 females), whose ages ranged from 20 to 70, and most of whom were sufferers from endogenous depressions. For the first three to five days the drug was administered intramuscularly with a maximum daily dose of 100 to 150 mg. The drug was then given orally in a maximum daily dose of 300 to 375 mg. Treatment was continued for at least thirty days. An assessment of the results shows that 15 had complete remissions, and 22 showed considerable improvement. The five who showed no response were all severe cases with catatonia and they responded to electroconvulsive therapy. The results were related more closely to the duration of treatment than to the dosage. Side-effects, which were never serious, included dryness of the mouth, moderate tachycardia, disturbances of accommodation (8%), hypotension, and sweating (18%). In the opinion of Dr. Fazio and his colleagues the great advantage of this new drug is that it reduces the number of cases in which it is necessary to use electro-convulsive therapy.

Dupuytren's contracture.—According to G. Mars, M. Morpurgo and L. De Ponti, Dupuytren's contracture is the result of compression of the nerve roots due to narrowing of the cervical intervertebral spaces. They base their conclusion upon a radiological study of 22 cases, whose ages ranged from 50 to 94, using as controls 20 normal individuals of the same age distribution. This study showed that in every one of the 22 patients with Dupuytren's contracture there was appreciable narrowing of the intervertebral spaces, whereas these were normal in all the controls. The narrowing was most marked in the case of the 5th, 6th and 7th spaces: i.e. those through which pass the nerve roots from which the brachial plexus is formed. In unilateral cases they found that the cervical vertebral lesions were localized to the affected side of the body.

Prevention of transfusion reactions.—The routine administration of chlorpromazine is recommended by E. Grossi as a means of preventing transfusion reactions. This recommendation is based upon his experience in a series of 724 transfusions—with whole blood, plasma, or plasma substitutes—in only one of which did a febrile reaction occur. The only side-effect—and that a minor one—was the degree of sleepiness induced in some of the patients.

Radiotherapy in syringomyelia.—In a series of 28 cases of syringomyelia, M. Marcato and A. Maestri report improvement in 14 cases (50%), and stabilization of symptoms in 12 cases (42.8%) as a result of deep x-ray therapy. Treatment consisted of a total dose of 1000r to 1500r, administered in 10 sessions, and in two fields for each area irradiated.

The problem of glomerulonephritis.—The problem of the clinical evolution of glomerulonephritis has recently been reviewed by Professor L. Migone, of the University of Parma, in which he stresses the unpredictability of the disease. In some cases there is a rapid steadily progressive development of the disease from the acute to the chronic stage. In others this progression is so slow and intermittent that often there is no apparent connexion between the acute and the chronic stage. He insists that there is no correlation between the severity of the acute phase of the disease and the tendency for the disease to become chronic. This, he stresses, is what makes it so difficult to give a prognosis in acute glomerulonephritis.

He discusses the evidence purporting to show the presence of renal antibodies in glomerulonephritis, but he does not consider that, to date, this evidence justifies the conclusion that chronic glomerulonephritis is due to auto-immunization to the patient's own renal tissues.

'Notes from the Continent' are produced in collaboration with the Editors of Bruxelles-Médical *(Belgium)*, La Revue du Praticien *(France)*, Münchener Medizinische Wochenschrift *(Germany)*, and Minerva Medica *(Italy)*.

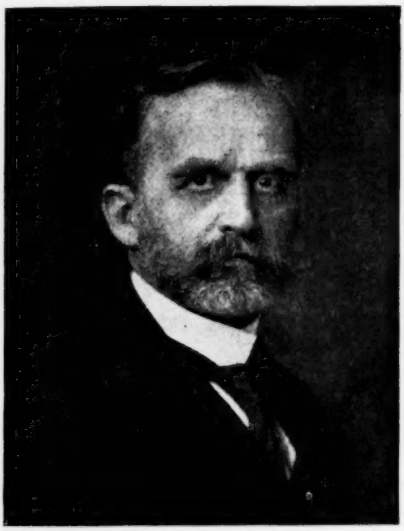
THE PRACTITIONER

Fifty Years Ago

'He speaks holiday'.—Shakespeare: *The Merry Wives of Windsor*. Act iii, sc. 2, l. 69.

NOVEMBER, 1908

'THOSE of us who have been able to take holidays this year have now returned to work, and can bring the light of experience to bear upon any question that may arise as to the value of vacations in keeping mind and body healthy'. Part



Hermann Rieder, M.D. (1858-1932).

of the Editor's holiday 'was spent in reading a book by a French physician . . . who maintained that holidays did more harm than good, and that we could perfectly well stick to our work all the year round without interruption. Very likely we could, if certain conditions could be guaranteed: if the circumstances of the work were hygienic, if we were thoroughly interested in it, if we never worked under high pressure, and if we took mild, regular exercise. But those conditions are very seldom present, and it is precisely on their absence that the case for holidays depends. The number of men, in a position to decide for themselves exactly how hard they will work, is very small indeed; and they, working because they like it, are specially liable to work longer hours than are good for them. They need, therefore, just as much as the others, to be dragged away from their desks and sent out into the fields with golf clubs, fishing rods, ice-axes, or other sporting implements in their hands. Even if they resent the change of occupation at first, it will do them good. . . . A defence of holidays, indeed, if other defences were wanting, might be constructed on the same lines of Matthew Arnold's famous defence of wine. "Wine", said the great thinker, "adds to the enjoyableness of life, and whatever adds to the enjoyableness of life adds to its richness, and fulness". The aphorism is not perhaps one fit for absolutely universal application. It does certainly seem to lend itself to abuse on the part of a voluptuary. But we may apply it, in moderation, to holidays without any fear of the consequences'.

Under the heading 'Infanticide', 'Notes by the Way' say of a circular letter addressed from the Home Office to the persons who have interested themselves in the case of Daisy Lord, that it 'will not satisfy the more hysterical section of those whom it is hardly an exaggeration to describe as her "supporters". From some of of their indignant communications to the Press, one would suppose them to believe that the unfortunate girl had become a mother accidentally, as she might have caught a cold or sprained her ankle, and had committed infanticide either in a fit of absence of mind or for the purpose of drawing attention to the injustices of a social system under which women have to pay the penalty of the faults of men. They have . . . written of her as of a virgin martyr, while, at the same time, clamouring for the head of a victim of the other sex. That will not do. It would not do even if the infanticide could not identify the partner in her original fault; and the fact that she does not identify him is strong presumptive evidence that she was careless, irresponsible, and promiscuous in her amours. Nor is the fact that the temptation to infanticide is in certain cases a strong reason for leaving it unpunished. It is, in fact, rather a reason to the contrary'.

Nestor Tirard, M.D., F.R.C.P., Professor of Medicine, King's College, begins his article on 'Infective or Ulcerative Endocarditis': 'In medical practice, there are few diseases which create greater anxiety than infective or ulcerative endocarditis. When recognized during life, the prognosis is necessarily grave, but unfortunately the mode of onset, and the prominent symptoms often present the utmost variations, and it is frequently almost impossible to avoid forming an erroneous diagnosis'. Sir Nestor

Tirard (1853-1928) was appointed physician to King's College Hospital in 1892, was professor of pharmacology from 1885 to 1900, and of medicine for the next nineteen years, and served as secretary of the Pharmacopœia Committee of the General Medical Council from 1895 to 1915. He was knighted in 1916.

W. J. Fenton, M.D., F.R.C.P., Assistant Physician, Charing Cross Hospital and Hospital for Consumption and Diseases of the Chest, Brompton, writes on 'Adherent Pericardium', and L. H. L. Mackenzie, M.B., B.C., contributes a 33-page article on 'Gastric Ulcer'.

In his review of some recent work on the stomach, F. Craven Moore, M.D., M.R.C.P., Lecturer in Medicine, University of Manchester, refers to Rieder as being the first successfully to employ Cannon's x-ray method in investigating the human stomach during life. Hermann Rieder, who was born at Rosenheim in Bavaria a century ago on December 3, 1858, graduated M.D. at Munich in 1883. A radiologist of international repute, he introduced contrast media for examining the gastro-intestinal tract (1904-10) and in 1909 published his classic paper on gastro-intestinal cinematography. Some of the forms of the stomach associated with his name are described by Craven Moore. Rieder died in 1932.

'A Manual of Venereal Diseases' by Officers of the Royal Army Medical Corps 'is modestly designated as a convenient manual for officers of the R.A.M.C., but to anyone interested in the study and treatment of syphilis, it cannot fail to be of the greatest value, and it is, further, an eloquent testimony to the untiring efforts of military surgeons in the elucidation of the difficult problems of the treatment and prophylaxis of Venereal Diseases in the Army'.

If C. Lloyd Tuckey's 'Treatment by Hypnotism and Suggestion' 'were widely read by medical men, it would be decidedly to the advantage of both the profession and their patients. . . . Nobody, who is up to date in his medical reading, can now deny that hypnotism must be classed as a therapeutic agent of great value, and, in the hands of a conscientious medical man, no serious harm is likely to follow'.

'Preparations and Inventions' describe 'Arsacetin and Sabromin' (Meister, Lucius & Brüning Ltd.) and 'Silcool', a vegetable silk-wool for stuffing mattresses (Thomas Heard).

W.R.B.

ST. ANDREWS HOSPITAL, NORTHAMPTON

FOR NERVOUS AND MENTAL DISORDERS

President—THE EARL SPENCER

Medical Superintendent—THOMAS TENNENT, M.D., F.R.C.P., D.P.H., D.P.M.

This Registered Hospital is situated in 130 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders, or who wish to prevent recurrent attacks of mental trouble; temporary patients, and certified patients of both sexes are received for treatment. Careful clinical, biochemical, bacteriological and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches can be provided.

WANTAGE HOUSE

This is a Reception Hospital in detached grounds with a separate entrance, to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods; insulin treatment is available for suitable cases. There is an Operating Theatre, a Dental Surgery, an X-Ray Room, an Ultra-Violet Apparatus, and a Department for Diathermy and High-Frequency treatment. It also contains Laboratories for biochemical, bacteriological, and pathological research. Psychotherapeutic treatment is employed when indicated.

MOULTON PARK

Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit, and vegetables are supplied to the Hospital from the farm, gardens, and orchards of Moulton Park. Occupational therapy is a feature of this branch, and patients are given every facility for occupying themselves in farming, gardening, and fruit-growing.

BRYN-Y-NEUADD HALL

The seaside house of St. Andrews Hospital is beautifully situated in a Park of 330 acres, at Llanfairfechan amidst the finest scenery in North Wales. On the north-west side of the Estate a mile of sea coast forms the boundary. Patients may visit this branch for a short seaside change, or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout fishing in the park.

At all the branches of the Hospital there are cricket grounds, football and hockey grounds, lawn tennis courts (grass and hard courts), croquet grounds, golf courses, and bowling greens. Ladies and gentlemen have their own gardens, and facilities are provided for handicrafts, such as carpentry, &c.

For terms and further particulars apply to the Medical Superintendent (Telephone: No. 4354, three lines, Northampton), who can be seen in London by appointment.